=> fil hcap

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FILE COVERS 1907 - 4 Jan 2005 VOL 142 ISS 2
FILE LAST UPDATED: 3 Jan 2005 (20050103/ED)

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=> fil medlin

FILE 'MEDLINE' ENTERED AT 10:37:55 ON 04 JAN 2005

FILE LAST UPDATED: 1 JAN 2005 (20050101/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
MeSH 2005 vocabulary. See http://www.nlm.nih.gov/mesh/ and
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
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RECORDS LAST ADDED: 29 December 2004 (20041229/ED)

FILE RELOADED: 19 October 2003.

=> fil pascal

FILE 'PASCAL' ENTERED AT 10:38:00 ON 04 JAN 2005

FILE LAST UPDATED: 23 DEC 2004 <20041223/UP>
FILE COVERS 1977 TO DATE.

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FILE COVERS 1985 TO 3 JAN 2005 (20050103/ED)

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=> fil embas

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FILE COVERS 1973 TO 18 Nov 2004 (20041118/ED)

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    HIT STRUCTURES WITHIN THE BIBLIOGRAPHIC DOCUMENT  <<<

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    Derwent Chemistry Resource display fields  <<<

>>> THE CPI AND EPI MANUAL CODES HAVE BEEN REVISED FROM UPDATE 200501.
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Dec 17, 2004 (20041217/UP).

=> d que l114
L81 (       124)SEA FILE=HCAPLUS ABB=ON  PLU=ON  ISHIYAMA, N?/AU
L82 (        40)SEA FILE=HCAPLUS ABB=ON  PLU=ON  ISHIGE, H?/AU
L83 (       452)SEA FILE=HCAPLUS ABB=ON  PLU=ON  MIMURA, M?/AU
L84 (      1383)SEA FILE=HCAPLUS ABB=ON  PLU=ON  OKUNO, T?/AU
L85 (       363)SEA FILE=HCAPLUS ABB=ON  PLU=ON  UKAI, K?/AU
L86 (        23)SEA FILE=HCAPLUS ABB=ON  PLU=ON  KIYOFUJI, T?/AU
L87 (        54)SEA FILE=HCAPLUS ABB=ON  PLU=ON  TAUCHI, S?/AU
L88 (       143)SEA FILE=HCAPLUS ABB=ON  PLU=ON  INOGUCHI, K?/AU
L89 (      2490)SEA FILE=HCAPLUS ABB=ON  PLU=ON  HUANG, P?/AU
L90 (       391)SEA FILE=HCAPLUS ABB=ON  PLU=ON  LOEW, G?/AU
L91 (      6616)SEA FILE=HCAPLUS ABB=ON  PLU=ON  ?SECRETAGOG?
L92           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L81 OR L82 OR L83 OR L84 OR
                L85 OR L86 OR L87 OR L88 OR L89 OR L90) AND L91
L109         12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MAKI, L?/AU
L110      46322 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ?GROWTH?(2W)?HORMON?
L111          0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L109 AND L110
L112          4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L111 OR L92
L113          0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L109 AND ?SECRETAGOG?
L114          4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L112 OR L113


=>
     (FILE 'MEDLINE, BIOSIS, PASCAL, JICST-EPLUS, EMBASE, CONFSCI, WPIX'
     ENTERED AT 10:22:44 ON 04 JAN 2005)

=> d que l108
L93          489 SEA ISHIYAMA, N?/AU
L94          184 SEA ISHIGE, H?/AU
L95         1442 SEA MIMURA, M?/AU
L96         4407 SEA OKUNO, T?/AU
L97         1328 SEA UKAI, K?/AU
L98           38 SEA KIYOFUJI, T?/AU
L99           53 SEA TAUCHI, S?/AU
L100         247 SEA INOGUCHI, K?/AU
```

```
L101       4872 SEA HUANG, P?/AU
L102        669 SEA LOEW, G?/AU
L103         75 SEA MAKI, L?/AU
L104     186505 SEA ?GROWTH?(2W) ?HORMON?
L105      20952 SEA ?SECRETAGOG?
L106       2348 SEA L104 (7A) L105
L107          6 SEA (L93 OR L94 OR L95 OR L96 OR L97 OR L98 OR L99 OR L100 OR
                L101 OR L102 OR L103) AND L106
L108          3 DUP REM L107 (3 DUPLICATES REMOVED)


=> dup rem l114 l108

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PROCESSING COMPLETED FOR L114
PROCESSING COMPLETED FOR L108
L116          4 DUP REM L114 L108 (3 DUPLICATES REMOVED)
                ANSWERS '1-4' FROM FILE HCAPLUS

=> d ibib abs ed 1-
YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

L116 ANSWER 1 OF 4  HCAPLUS  COPYRIGHT 2005 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2003:209423  HCAPLUS
DOCUMENT NUMBER:          139:47400
TITLE:                    The role of circulating ghrelin in growth hormone (GH)
                          secretion in freely moving male rats
AUTHOR(S):                Okimura, Yasuhiko; Ukai, Kiyoharu; Hosoda,
                          Hiroshi; Murata, Masahiro; Iguchi, Genzo; Iida, Keiji;
                          Kaji, Hidesuke; Kojima, Masayasu; Kangawa, Kenji;
                          Chihara, Kazuo
CORPORATE SOURCE:         Department of Basic Allied Medicine, Kobe University
                          School of Medicine, Kobe, Suma, 654-0142, Japan
SOURCE:                   Life Sciences (2003), 72(22), 2517-2524
                          CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER:                Elsevier Science Inc.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   To examine the physiol. significance of plasma ghrelin in generating
     pulsatile growth hormone (GH) secretion in rats, plasma GH and ghrelin
     levels were determined in freely moving male rats.  Plasma GH was pulsatility
     secreted as reported previously.  Plasma ghrelin levels were measured by
     both N-RIA recognizing the active form of ghrelin and C-RIA determining total
     amount of ghrelin.  Plasma ghrelin levels determined by N-RIA and C-RIA were
21.6
     and 315.5 pM, resp., during peak periods when plasma GH levels were
     greater than 100 ng/mL.  During trough periods when plasma GH levels were
     less than 10 ng/mL, they were 16.5 and 342.1 pM, resp.  There were no
     significant differences in plasma ghrelin levels between two periods.
```

Next, effect of a GH **secretagogue** antagonist, [DLys 3]-GHRP-6, on plasma GH profiles was examined There were no significant differences in both peak GH levels and area under the curves of GH (AUCs) between [DLys 3]-GHRP-6-treated and control rats. These findings suggest circulating ghrelin in peripheral blood does not play a role in generating pulsatile GH secretion in freely moving male rats.

ED Entered STN: 18 Mar 2003
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L116 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2001:758461 HCAPLUS
DOCUMENT NUMBER: 136:63596
TITLE: Rational design, discovery, and synthesis of a novel series of potent growth hormone **secretagogues**
AUTHOR(S): **Huang, Ping**; **Loew, Gilda H.**; Funamizu, Hidenori; **Mimura, Mitsuo**; **Ishiyama, Nobuo**; Hayashida, Mitsuo; **Okuno, Tadashi**; Shimada, Osafumi; Okuyama, Akihiko; Ikegami, Satoru; Nakano, Jun; **Inoguchi, Kiyoshi**
CORPORATE SOURCE: Molecular Research Institute, Mountain View, CA, 94043, USA
SOURCE: Journal of Medicinal Chemistry (2001), 44(24), 4082-4091
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the joint exptl. and computational efforts reported here to obtain novel chemical entities as growth hormone **secretagogues** (GHSs), a small database of peptides and non-peptides known to have GHS activity was used to generate and assess a 3D pharmacophore for this activity. This pharmacophore was obtained using a systematic and efficient procedure, "DistComp", developed in the authors' laboratory The 3D pharmacophore identified was then used to search 3D databases to explore chemical structures that could be novel GHSs. A number of these were chosen for synthesis and assessment of their ability to release growth hormone (GH) from rat pituitary cells. Among the compds. tested, those with a benzothiazepin scaffold were discovered with micromolar activity. To facilitate lead optimization, a second program, a site-dependent fragment QSAR procedure was developed. This program calcs. a library of chemical and phys. properties of "fragments" or chemical components in a known pharmacophore and dets. which, if any, of these properties are important for the observed activity. The combined use of the 3D pharmacophore and the results of the site-dependent fragment QSAR anal. led to the discovery and synthesis of a novel series of potent GHSs, a number of which had nanomolar in vitro activity.

ED Entered STN: 18 Oct 2001
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L116 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2000:592574 HCAPLUS
DOCUMENT NUMBER: 133:193493
TITLE: Preparation of novel peptidomimetics as growth hormone **secretagogues**
INVENTOR(S): **Ishiyama, Nobuo**; **Ishige, Hirohide**; **Mimura, Mitsuo**; **Okuno, Tadashi**; **Ukai, Kiyoharu**; **Kiyofuji, Takeshi**;

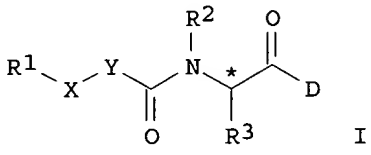
Tauchi, Shinji; Inoguchi, Kiyoshi;
Huang, Ping; Loew, Gilda H.
PATENT ASSIGNEE(S): Kaken Pharmaceutical Co., Ltd., Japan; Molecular Research Institute

SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

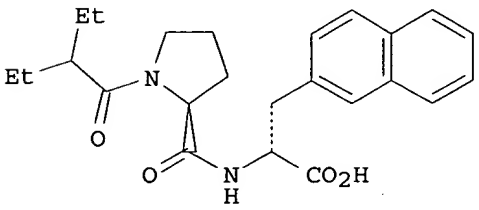
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000048623	A1	20000824	WO 2000-US4001	20000217
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2362290	AA	20000824	CA 2000-2362290	20000217
EP 1158996	A1	20011205	EP 2000-921329	20000217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002542151	T2	20021210	JP 2000-599413	20000217
AU 759022	B2	20030403	AU 2000-41671	20000217
PRIORITY APPLN. INFO.:			US 1999-251734 A	19990218
			WO 2000-US4001 W	20000217

OTHER SOURCE(S): MARPAT 133:193493

GI



I



II

AB The title compds. [I; R1 = (un)substituted alkyl, cycloalkyl, alkoxy, etc.; X = CO, SO2; Y = NR4(CH2)nCR5R6 (wherein n = 0-4; R4 = H, (un)substituted alkyl, cycloalkyl, aryl; R5, R6 = H, alkyl; or R5 and R6 or R4 and R5 are taken together to form (un)substituted alkylene); R2 = H, alkyl; R3 = (un)substituted alkyl, cycloalkyl, aryl; D = (un)substituted

NH2, alkoxy, alkylthio; * represents an asym. center] and their pharmaceutically acceptable salts which have growth hormone releasing activity in humans or animals, were prepared E.g., a multi-step synthesis of II.HCl which showed growth hormone releasing activity in primary rat anterior pituitary cells below 10-8 M, was given.

ED Entered STN: 25 Aug 2000

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L116 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:495469 HCAPLUS

DOCUMENT NUMBER: 141:82695

TITLE: Phospholipase D1 Regulates **Secretagogue** -stimulated Insulin Release in Pancreatic β-Cells

AUTHOR(S): Hughes, William E.; Elgundi, Zehra; **Huang, Ping**; Frohman, Michael A.; Biden, Trevor J.

CORPORATE SOURCE: Cell Signalling Group, The Garvan Institute of Medical Research, Sydney, 2010, Australia

SOURCE: Journal of Biological Chemistry (2004), 279(26), 27534-27541
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Phospholipase D (PLD) has been strongly implicated in the regulation of Golgi trafficking as well as endocytosis and exocytosis. Our aim was to investigate the role of PLD in regulating the biphasic exocytosis of insulin from pancreatic β-cells that is essential for mammalian glucose homeostasis. We observed that PLD activity in MIN6 pancreatic β-cells is closely coupled to secretion. Cellular PLD activity was increased in response to a variety of **secretagogues** including the nutrient glucose and the cholinergic receptor agonist carbamoylcholine. Conversely, pharmacol. or hormonal inhibition of stimulated secretion reduced PLD activity. Most importantly, blockade of PLD-catalyzed phosphatidic acid formation using butan-1-ol inhibited insulin secretion in both MIN6 cells and isolated pancreatic islets. It was further established that PLD activity was required for both the first and the second phase of glucose-stimulated insulin release, suggesting a role in the very distal steps of exocytosis, beyond granule recruitment into a readily releasable pool. Visualization of granules using green fluorescent protein-phogrin confirmed a requirement for PLD prior to granule fusion with the plasma membrane. PLD1 was shown to be the predominant isoform in MIN6 cells, and it was located at least partially on insulin granules. Overexpression of wild-type or a dominant neg. catalytically inactive mutant of PLD1 augmented or inhibited **secretagogue**-stimulated secretion, resp. The results suggest that phosphatidic acid formation on the granule membrane by PLD1 is essential for the regulated secretion of insulin from pancreatic β-cells.

ED Entered STN: 18 Jun 2004

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> fil lreg

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DICTIONARY FILE UPDATES: 2 JAN 2005 HIGHEST RN 807298-39-1

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http://www.cas.org/ONLINE/DBSS/registryss.html

=> fil hcap

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FILE LAST UPDATED: 3 Jan 2005 (20050103/ED)

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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 4 Jan 2005 (20050104/PD)
FILE LAST UPDATED: 4 Jan 2005 (20050104/ED)
HIGHEST GRANTED PATENT NUMBER: US6839903
HIGHEST APPLICATION PUBLICATION NUMBER: US2004268457
CA INDEXING IS CURRENT THROUGH 4 Jan 2005 (20050104/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 4 Jan 2005 (20050104/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Oct 2004
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2004

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=> fil medlin

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FILE LAST UPDATED: 1 JAN 2005 (20050101/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
MeSH 2005 vocabulary. See http://www.nlm.nih.gov/mesh/ and
http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a
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=> fil biosis

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RECORDS LAST ADDED: 29 December 2004 (20041229/ED)

FILE RELOADED: 19 October 2003.

=> fil embas

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=> fil beilst

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FILE LAST UPDATED ON NOVEMBER 3, 2004

FILE COVERS 1771 TO 2004.
*** FILE CONTAINS 9,073,068 SUBSTANCES ***

>>>PLEASE NOTE: Reaction Data and substance data are stored in separate documents and can not be searched together in one query. Reaction data for BEILSTEIN compounds may be displayed immediately with the display codes PRE (preparations) and REA (reactions). A substance answer set retrieved after the search for a chemical name, a compounds with available reaction information by combining with PRE/FA, REA/FA or more generally with RX/FA. The BEILSTEIN Registry Number (BRN) is the link between a BEILSTEIN compound and belonging reactions. For mo detailed reaction searches BRNs can be searched as reaction partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

```
**********************************************************************
* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST.                *
* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE   *
* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE          *
* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS.                        *
* FOR PRICE INFORMATION SEE HELP COST                                *
**********************************************************************
```

NEW

*** PATENT NUMBERS (PN) AND BABS ACCESSION NUMBERS (BABSAN) CAN NOW BE SEARCHED, SELECTED AND TRANSFERRED.**

*** NEW DISPLAY FORMATS ALLREF, ALLP AND BABSAN SHOW ALL REFERENCES, ALL PATENT REFERENCES, OR ALL BABS ACCESSION NUMBERS FOR A COMPOUND AT A GLANCE.**

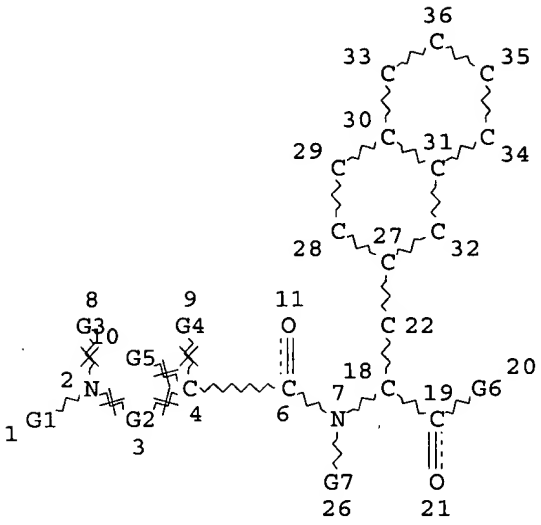
=> file stnguide

FILE 'STNGUIDE' ENTERED AT 10:31:32 ON 04 JAN 2005
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Dec 17, 2004 (20041217/UP).

=> d que l37
L20 STR

C@12 13 O O@14 S@15 O@16 C@17 N@23 O@24 S@25



VAR G1=12/15
REP G2=(0-6) C
VAR G3=H/17
VAR G4=H/17
VAR G5=H/17
VAR G6=23/24/25/17
VAR G7=H/17
NODE ATTRIBUTES:
NSPEC IS RC AT 2
NSPEC IS RC AT 4
NSPEC IS RC AT 12
NSPEC IS RC AT 14
NSPEC IS RC AT 15
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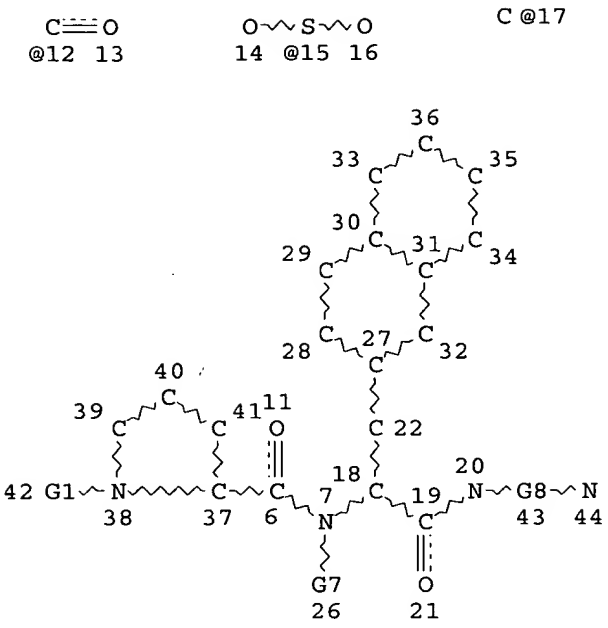
NSPEC IS RC AT 17
NSPEC IS RC AT 22
NSPEC IS RC AT 23
NSPEC IS RC AT 24
NSPEC IS RC AT 25
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 35

STEREO ATTRIBUTES: NONE
L22 7746779 SEA FILE=REGISTRY ABB=ON PLU=ON ((C6(S)C6)/ESS AND O>1 AND N>1) NOT ((PMS/CI) OR (SEQUENCE/FS))
L25 1501 SEA FILE=REGISTRY SUB=L22 SSS FUL L20
L35 STR



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REP G8=(0-10) C
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NSPEC IS RC AT 22
NSPEC IS RC AT 44
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 33

STEREO ATTRIBUTES: NONE
L37 372 SEA FILE=REGISTRY SUB=L25 SSS FUL L35

=> d l40
L40 ANALYZE L37 1- LC : 3 TERMS

TERM #	# OCC	# DOC	% DOC	LC
1	192	192	51.61	CA
2	192	192	51.61	CAPLUS
3	2	2	0.54	USPATFULL

********* END OF L40***

=> d que nos l39

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L20             STR
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L25        1501 SEA FILE=REGISTRY SUB=L22 SSS FUL L20
L35             STR
L37         372 SEA FILE=REGISTRY SUB=L25 SSS FUL L35
L39           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L37


=> d que nos l41
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L25        1501 SEA FILE=REGISTRY SUB=L22 SSS FUL L20
L35             STR
L37         372 SEA FILE=REGISTRY SUB=L25 SSS FUL L35
L41           1 SEA FILE=USPATFULL ABB=ON  PLU=ON  L37


=> d que nos l66
L20             STR
L22     7746779 SEA FILE=REGISTRY ABB=ON  PLU=ON  ((C6(S)C6)/ESS AND O>1 AND
                N>1) NOT ((PMS/CI) OR (SEQUENCE/FS))
L25        1501 SEA FILE=REGISTRY SUB=L22 SSS FUL L20
L35             STR
L37         372 SEA FILE=REGISTRY SUB=L25 SSS FUL L35
L59             SEL  PLU=ON  L37 1- CHEM :     374 TERMS
L60           0 SEA L59
L61      158023 SEA (?GROWTH? (2W) ?HORMON?)
L62       18196 SEA ?SECRETAGOG?
L63        1895 SEA L61 (5A) L62
L64          19 SEA L63 (L) (AMIDE OR ?ALANINAMID?)
L65          10 DUP REM L64 (9 DUPLICATES REMOVED)
L66          10 SEA L65 OR L60


=> d que l71
L67        4517 SEA FILE=WPIX ABB=ON  PLU=ON  (?GROWTH?(2W)?HORMON?)/BIX
L68         298 SEA FILE=WPIX ABB=ON  PLU=ON  (?SECRETAGOG? OR ?SECRET
                AGOG?)/BIX
L69         196 SEA FILE=WPIX ABB=ON  PLU=ON  L67 AND L68
L70       16474 SEA FILE=WPIX ABB=ON  PLU=ON  (C07-D03 OR B07-D03 OR E07-D03)/M
                C
L71          15 SEA FILE=WPIX ABB=ON  PLU=ON  L69 AND L70


=> dup rem l39 l41 l66 l71

FILE 'HCAPLUS' ENTERED AT 10:32:41 ON 04 JAN 2005
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FILE 'USPATFULL' ENTERED AT 10:32:41 ON 04 JAN 2005
CA INDEXING COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'MEDLINE' ENTERED AT 10:32:41 ON 04 JAN 2005

FILE 'BIOSIS' ENTERED AT 10:32:41 ON 04 JAN 2005
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FILE 'EMBASE' ENTERED AT 10:32:41 ON 04 JAN 2005

FILE 'WPIX' ENTERED AT 10:32:41 ON 04 JAN 2005

PROCESSING COMPLETED FOR L39
PROCESSING COMPLETED FOR L41
PROCESSING COMPLETED FOR L66
PROCESSING COMPLETED FOR L71
L115 28 DUP REM L39 L41 L66 L71 (1 DUPLICATE REMOVED)
ANSWERS '1-3' FROM FILE HCAPLUS
ANSWER '4' FROM FILE USPATFULL
ANSWERS '5-9' FROM FILE MEDLINE
ANSWERS '10-13' FROM FILE BIOSIS
ANSWER '14' FROM FILE EMBASE
ANSWERS '15-28' FROM FILE WPIX

=> file stnguide

FILE 'STNGUIDE' ENTERED AT 10:33:02 ON 04 JAN 2005

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Dec 17, 2004 (20041217/UP).

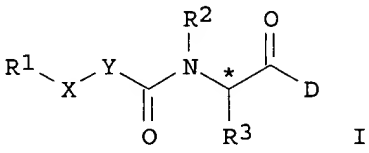
=> d ibib abs ed hitstr 1-3
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, USPATFULL, MEDLINE, BIOSIS, EMBASE, WPIX' - CONTINUE? (Y)/N:y

L115 ANSWER 1 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2000:592574 HCAPLUS
DOCUMENT NUMBER: 133:193493
TITLE: Preparation of novel peptidomimetics as growth hormone secretagogues
INVENTOR(S): Ishiyama, Nobuo; Ishige, Hirohide; Mimura, Mitsuo; Okuno, Tadashi; Ukai, Kiyoharu; Kiyofuji, Takeshi; Tauchi, Shinji; Inoguchi, Kiyoshi; Huang, Ping; Loew, Gilda H.
PATENT ASSIGNEE(S): Kaken Pharmaceutical Co., Ltd., Japan; Molecular Research Institute
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

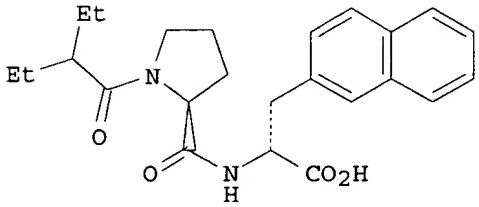
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000048623	A1	20000824	WO 2000-US4001	20000217

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,

AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
CA 2362290 AA 20000824 CA 2000-2362290 20000217
EP 1158996 A1 20011205 EP 2000-921329 20000217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
JP 2002542151 T2 20021210 JP 2000-599413 20000217
AU 759022 B2 20030403 AU 2000-41671 20000217
PRIORITY APPLN. INFO.: US 1999-251734 A 19990218
WO 2000-US4001 W 20000217
OTHER SOURCE(S): MARPAT 133:193493
GI



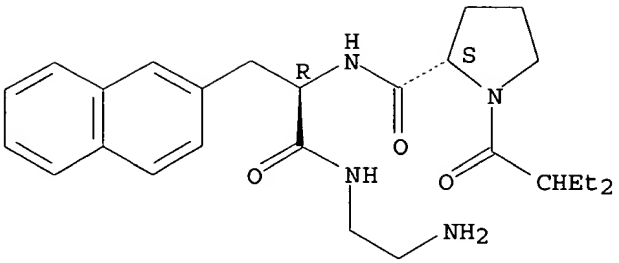
I



II

AB The title compds. [I; R1 = (un)substituted alkyl, cycloalkyl, alkoxy, etc.; X = CO, SO2; Y = NR4(CH2)nCR5R6 (wherein n = 0-4; R4 = H, (un)substituted alkyl, cycloalkyl, aryl; R5, R6 = H, alkyl; or R5 and R6 or R4 and R5 are taken together to form (un)substituted alkylene); R2 = H, alkyl; R3 = (un)substituted alkyl, cycloalkyl, aryl; D = (un)substituted NH2, alkoxy, alkylthio; * represents an asym. center] and their pharmaceutically acceptable salts which have growth hormone releasing activity in humans or animals, were prepared E.g., a multi-step synthesis of II.HCl which showed growth hormone releasing activity in primary rat anterior pituitary cells below 10-8 M, was given.
ED Entered STN: 25 Aug 2000
IT **289047-41-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of novel peptidomimetics as growth hormone secretagogues)
RN 289047-41-2 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-(2-aminoethyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

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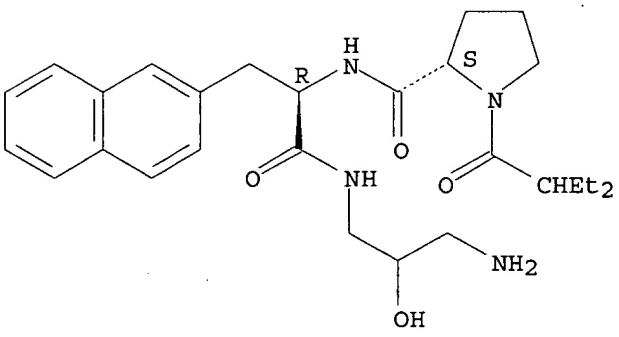
289050-93-7P 289477-13-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel peptidomimetics as growth hormone secretagogues)

RN 289047-03-6 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

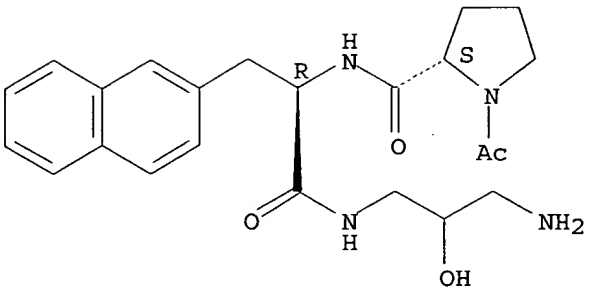
Absolute stereochemistry.



● HCl

RN 289047-04-7 HCAPLUS
CN D-Alaninamide, 1-acetyl-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

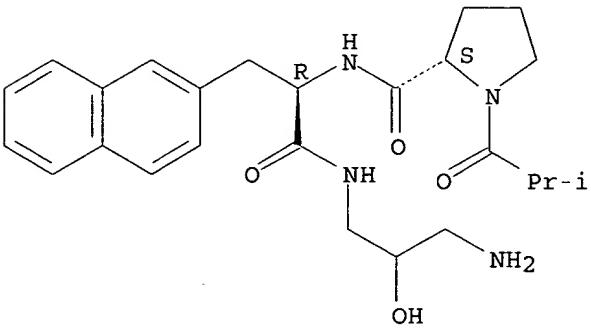
Absolute stereochemistry.



● HCl

RN 289047-05-8 HCAPLUS
CN D-Alaninamide, 1-(2-methyl-1-oxopropyl)-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

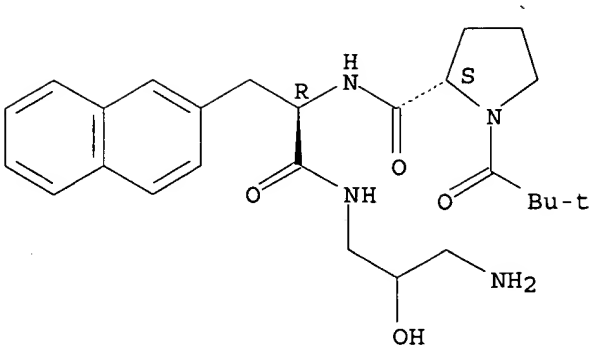
Absolute stereochemistry.



● HCl

RN 289047-06-9 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

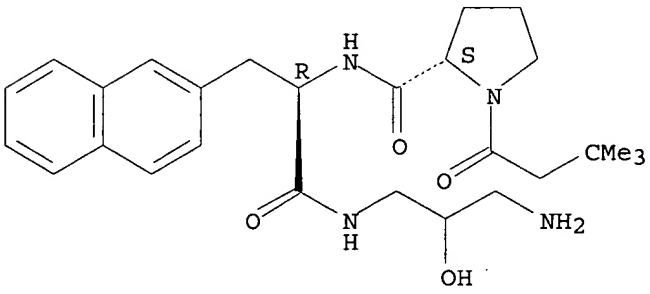
Absolute stereochemistry.



● HCl

RN 289047-07-0 HCAPLUS
CN D-Alaninamide, 1-(3,3-dimethyl-1-oxobutyl)-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

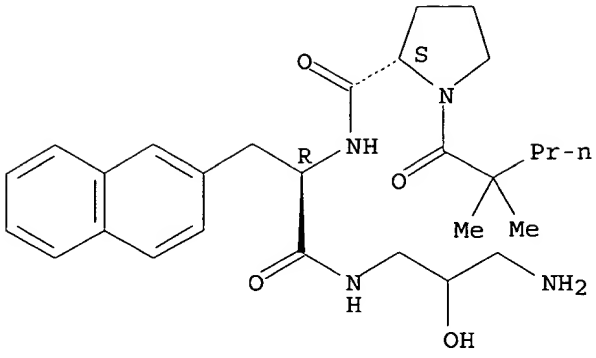
Absolute stereochemistry.



● HCl

RN 289047-08-1 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopentyl)-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

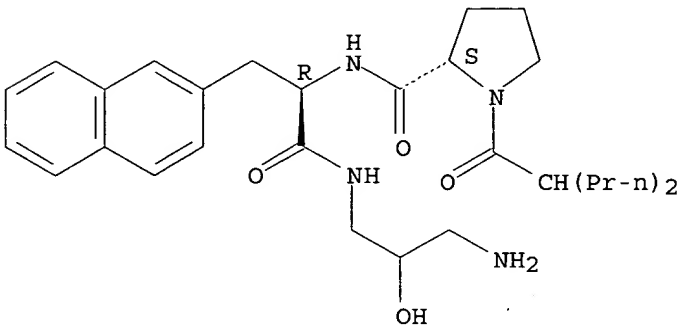
Absolute stereochemistry.



● HCl

RN 289047-09-2 HCAPLUS
CN D-Alaninamide, 1-(1-oxo-2-propylpentyl)-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

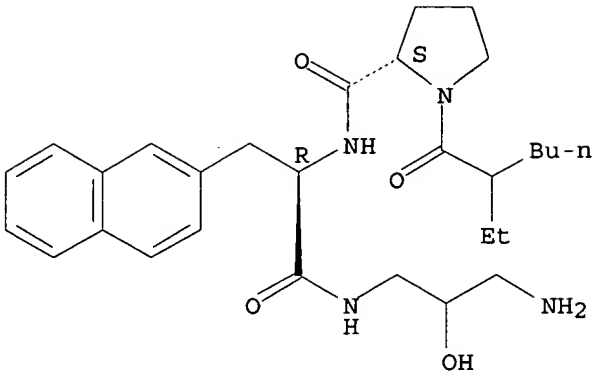
Absolute stereochemistry.



● HCl

RN 289047-10-5 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxohexyl)-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

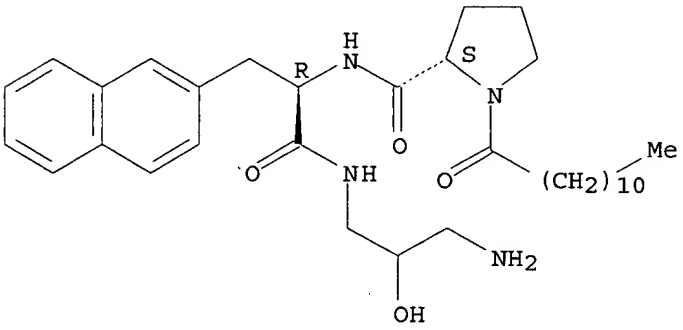
Absolute stereochemistry.



● HCl

RN 289047-11-6 HCAPLUS
CN D-Alaninamide, 1-(1-oxododecyl)-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

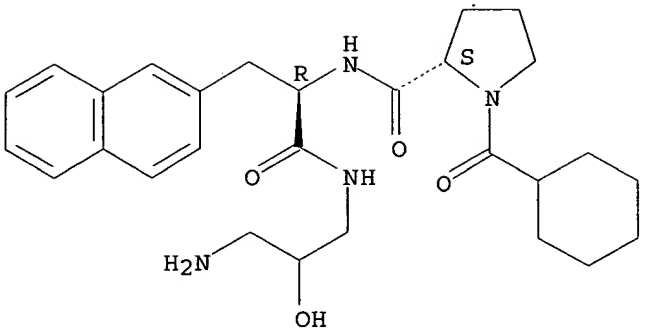
Absolute stereochemistry.



● HCl

RN 289047-12-7 HCAPLUS
CN D-Alaninamide, 1-(cyclohexylcarbonyl)-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

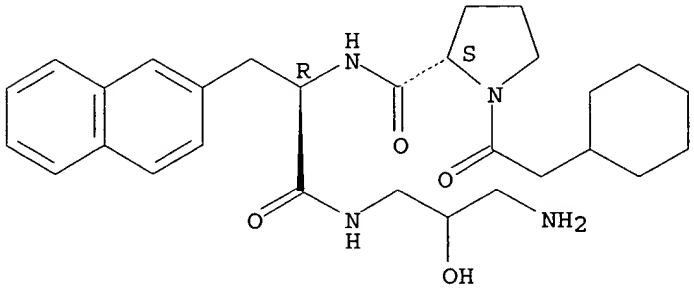
Absolute stereochemistry.



● HCl

RN 289047-13-8 HCAPLUS
CN D-Alaninamide, 1-(cyclohexylacetyl)-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

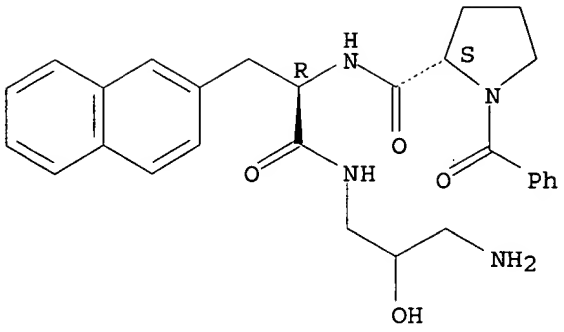
Absolute stereochemistry.



● HCl

RN 289047-14-9 HCAPLUS
CN D-Alaninamide, 1-benzoyl-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

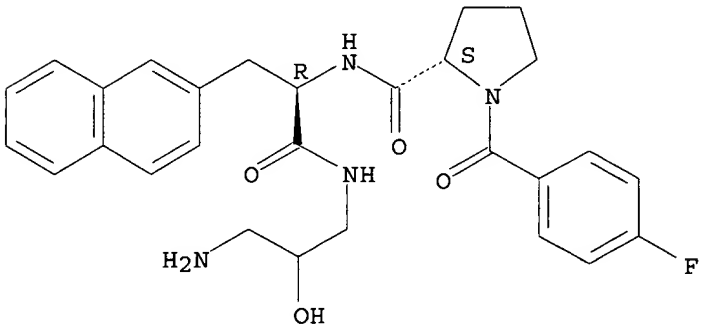
Absolute stereochemistry.



● HCl

RN 289047-15-0 HCAPLUS
CN D-Alaninamide, 1-(4-fluorobenzoyl)-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

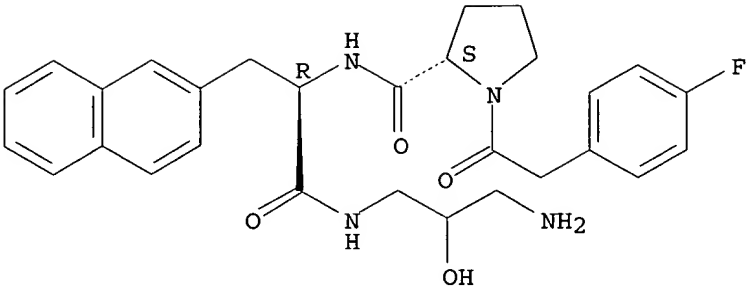
Absolute stereochemistry.



● HCl

RN 289047-16-1 HCAPLUS
CN D-Alaninamide, 1-[(4-fluorophenyl)acetyl]-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

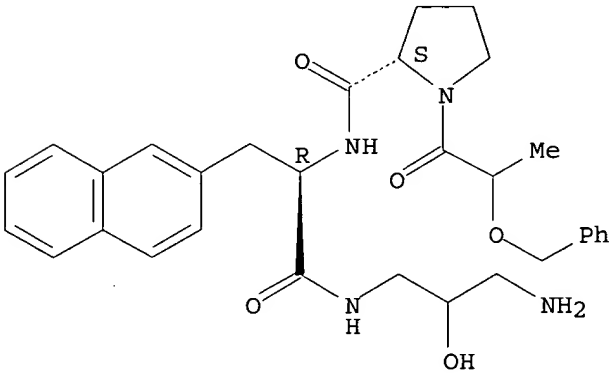
Absolute stereochemistry.



● HCl

RN 289047-17-2 HCAPLUS
CN D-Alaninamide, 1-[1-oxo-2-(phenylmethoxy)propyl]-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

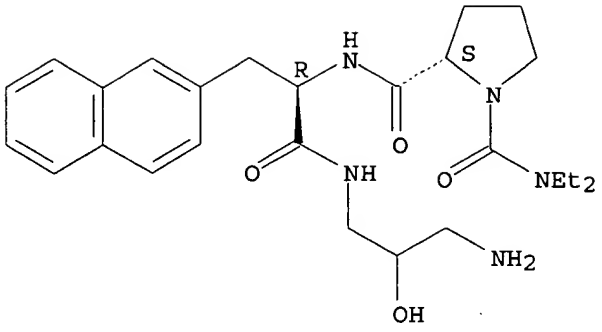
Absolute stereochemistry.



● HCl

RN 289047-18-3 HCAPLUS
CN D-Alaninamide, 1-[(diethylamino)carbonyl]-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

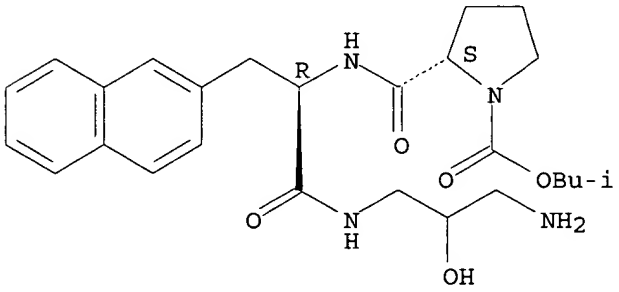
Absolute stereochemistry.



● HCl

RN 289047-19-4 HCAPLUS
CN D-Alaninamide, 1-[(2-methylpropoxy)carbonyl]-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

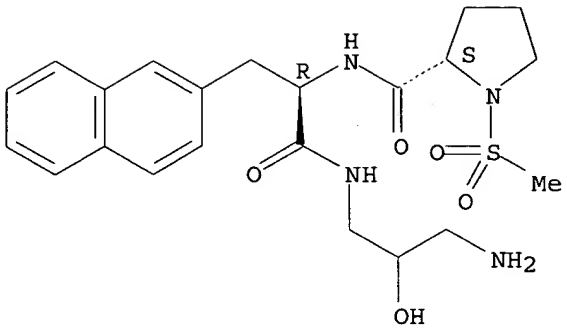
Absolute stereochemistry.



● HCl

RN 289047-20-7 HCAPLUS
CN D-Alaninamide, 1-(methylsulfonyl)-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

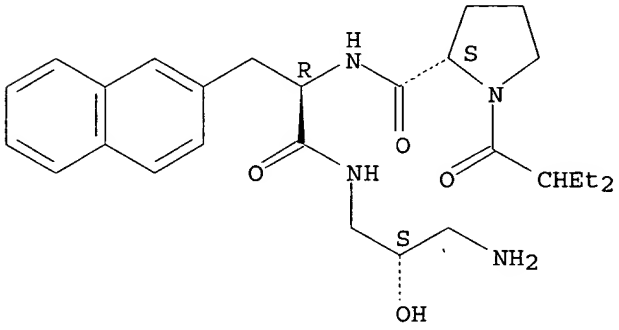
Absolute stereochemistry.



● HCl

RN 289047-21-8 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[(2S)-3-amino-2-hydroxypropyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

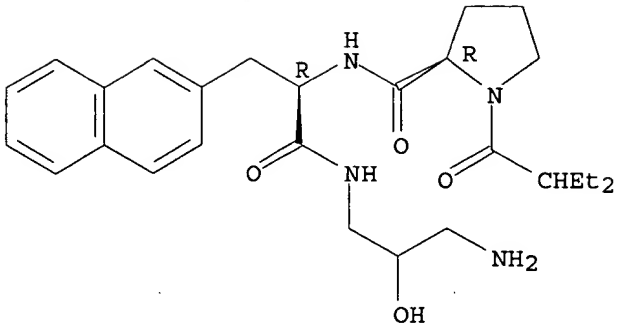
Absolute stereochemistry.



● HCl

RN 289047-22-9 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-D-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

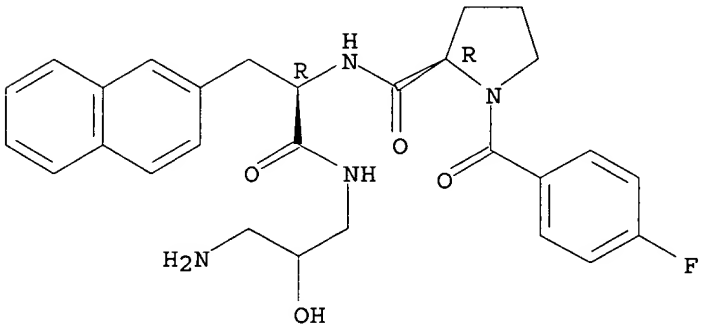
Absolute stereochemistry.



● HCl

RN 289047-23-0 HCAPLUS
CN D-Alaninamide, 1-(4-fluorobenzoyl)-D-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

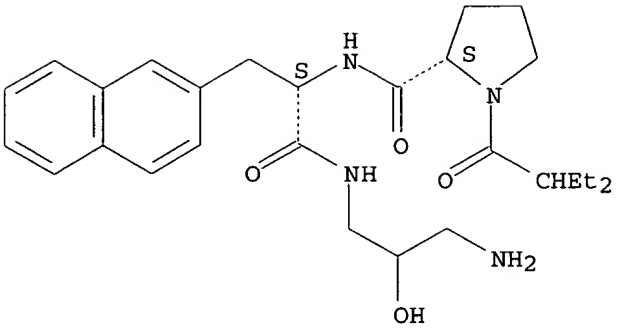
Absolute stereochemistry.



● HCl

RN 289047-24-1 HCAPLUS
CN L-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

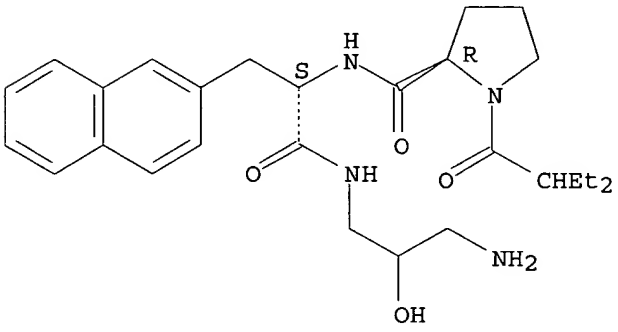
Absolute stereochemistry.



● HCl

RN 289047-25-2 HCAPLUS
CN L-Alaninamide, 1-(2-ethyl-1-oxobutyl)-D-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

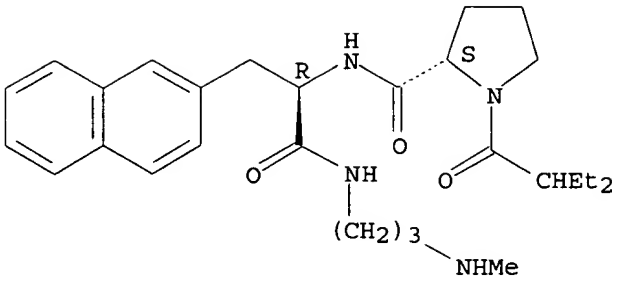
Absolute stereochemistry.



● HCl

RN 289047-29-6 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[3-(methylamino)propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

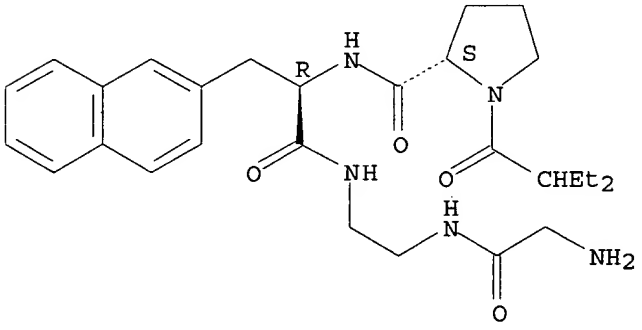
Absolute stereochemistry.



● HCl

RN 289047-30-9 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[2-[(aminoacetyl)amino]ethyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

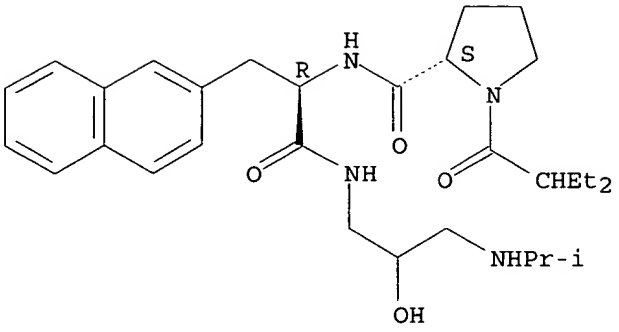
Absolute stereochemistry.



● HCl

RN 289047-31-0 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[2-hydroxy-3-[(1-methylethyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

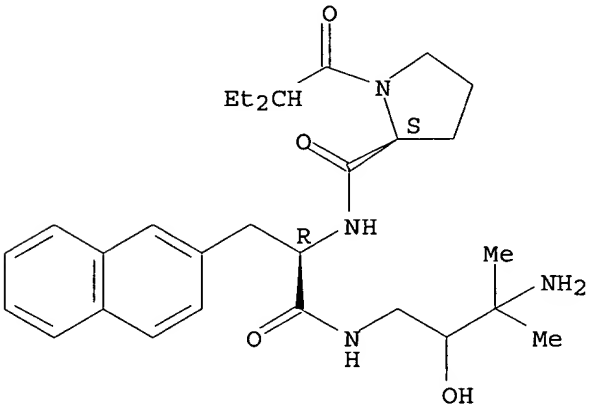
Absolute stereochemistry.



● HCl

RN 289047-33-2 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-(3-amino-2-hydroxy-3-methylbutyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

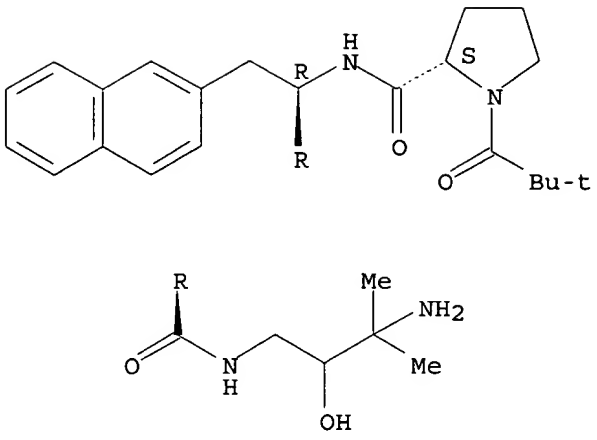
Absolute stereochemistry.



● HCl

RN 289047-34-3 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-(3-amino-2-hydroxy-3-methylbutyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

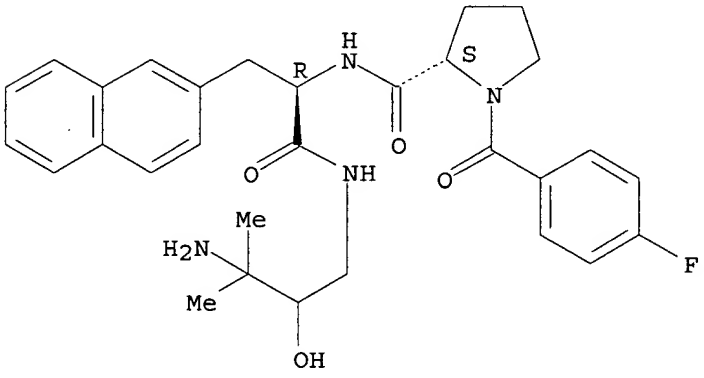
Absolute stereochemistry.



● HCl

RN 289047-35-4 HCAPLUS
CN D-Alaninamide, 1-(4-fluorobenzoyl)-L-prolyl-N-(3-amino-2-hydroxy-3-methylbutyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

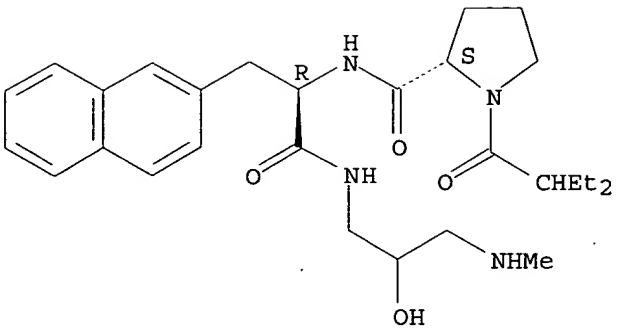
Absolute stereochemistry.



● HCl

RN 289047-36-5 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[2-hydroxy-3-(methylamino)propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

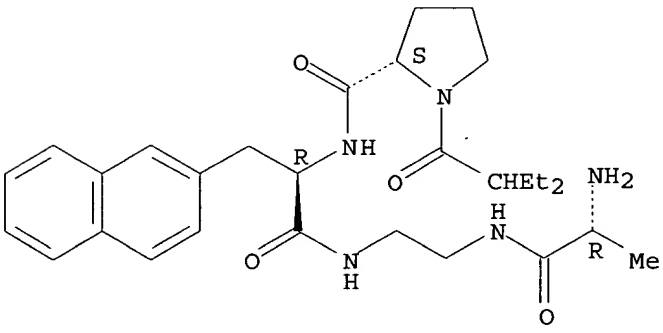
Absolute stereochemistry.



● HCl

RN 289047-37-6 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[2-[[(2R)-2-amino-1-oxopropyl]amino]ethyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

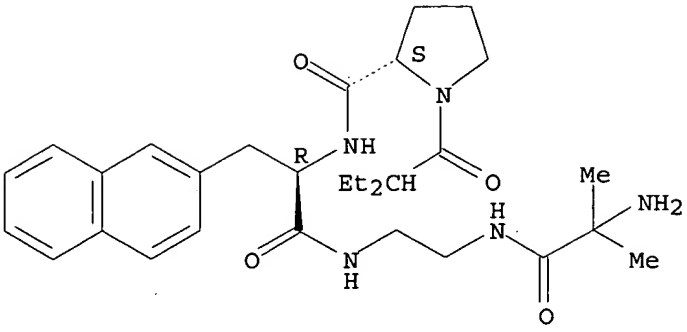
Absolute stereochemistry.



● HCl

RN 289047-38-7 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[2-[(2-amino-2-methyl-1-oxopropyl)amino]ethyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

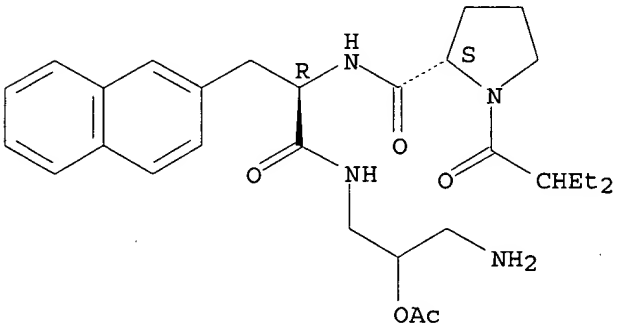
Absolute stereochemistry.



● HCl

RN 289047-39-8 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[2-(acetyloxy)-3-aminopropyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

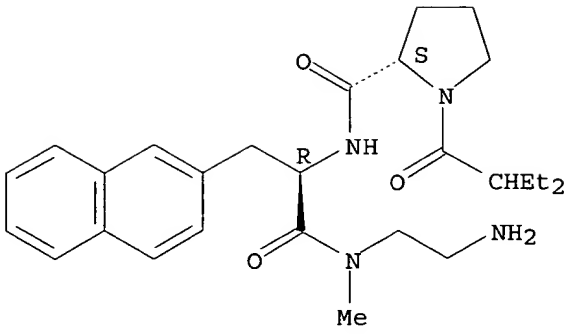
Absolute stereochemistry.



● HCl

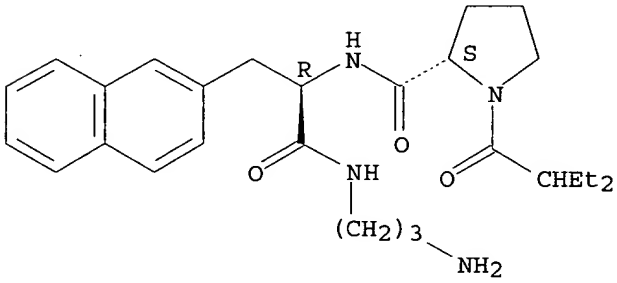
RN 289047-40-1 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-(2-aminoethyl)-N-methyl-3-(2-naphthalenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 289047-42-3 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-(3-aminopropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

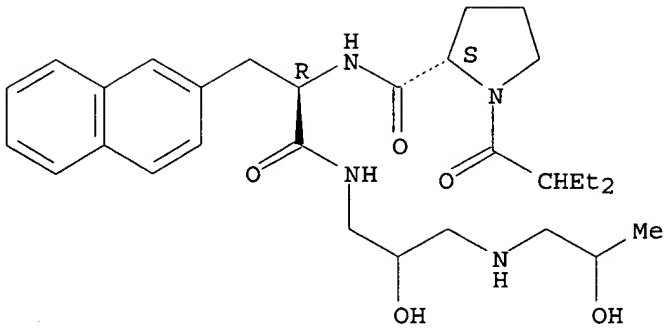
Absolute stereochemistry.



● HCl

RN 289047-88-7 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[2-hydroxy-3-[(2-hydroxypropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

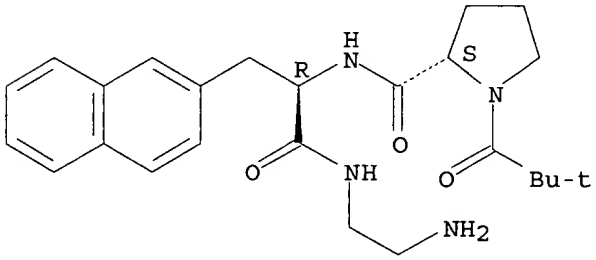
Absolute stereochemistry.



● HCl

RN 289047-89-8 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-(2-aminoethyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

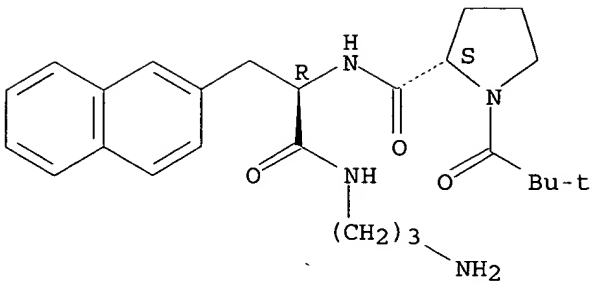
Absolute stereochemistry.



● HCl

RN 289047-90-1 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-(3-aminopropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

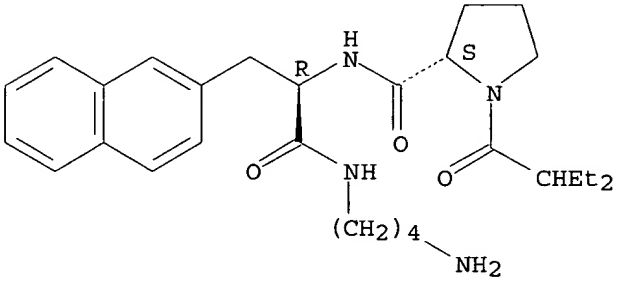
Absolute stereochemistry.



● HCl

RN 289047-91-2 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-(4-aminobutyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

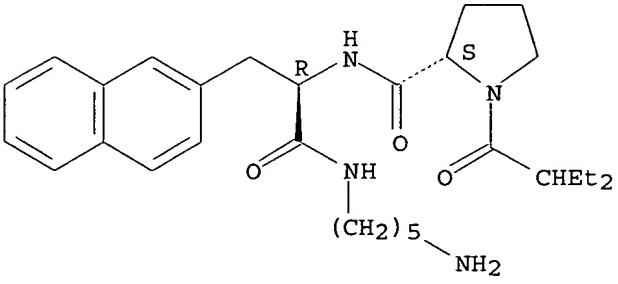
Absolute stereochemistry.



● HCl

RN 289047-92-3 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-(5-aminopentyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

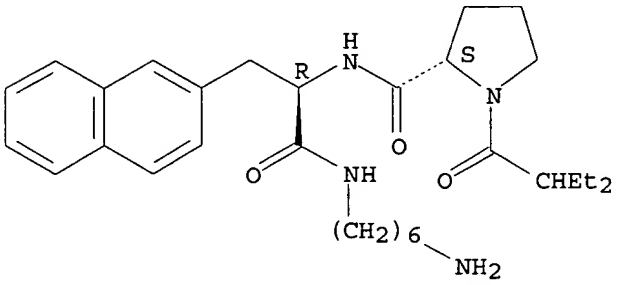
Absolute stereochemistry.



● HCl

RN 289047-93-4 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-(6-aminohexyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

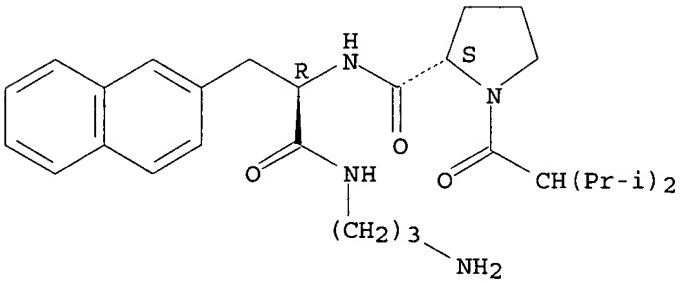
Absolute stereochemistry.



● HCl

RN 289047-94-5 HCAPLUS
CN D-Alaninamide, 1-[3-methyl-2-(1-methylethyl)-1-oxobutyl]-L-prolyl-N-(3-aminopropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

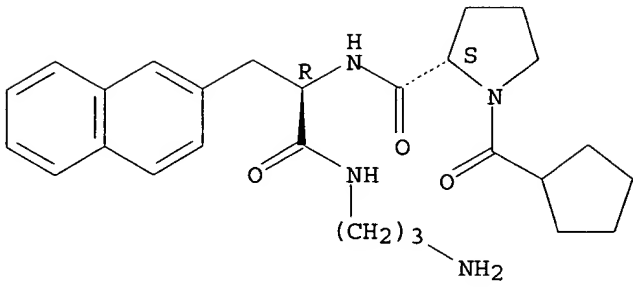
Absolute stereochemistry.



● HCl

RN 289047-95-6 HCAPLUS
CN D-Alaninamide, 1-(cyclopentylcarbonyl)-L-prolyl-N-(3-aminopropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

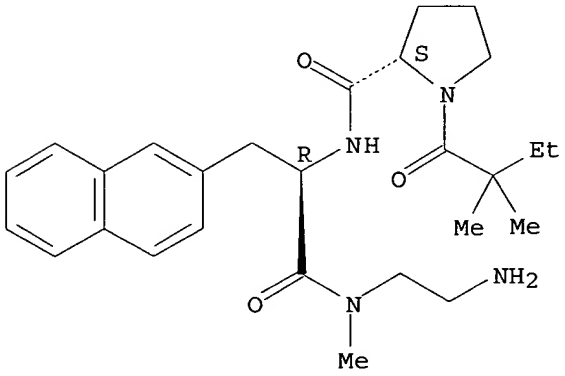
Absolute stereochemistry.



● HCl

RN 289047-96-7 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxobutyl)-L-prolyl-N-(2-aminoethyl)-N-methyl-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

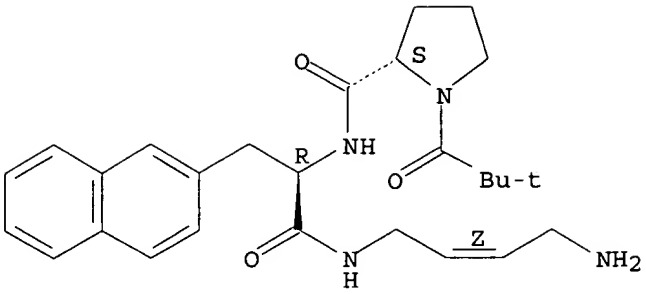
Absolute stereochemistry.



● HCl

RN 289047-97-8 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[(2Z)-4-amino-2-butenyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

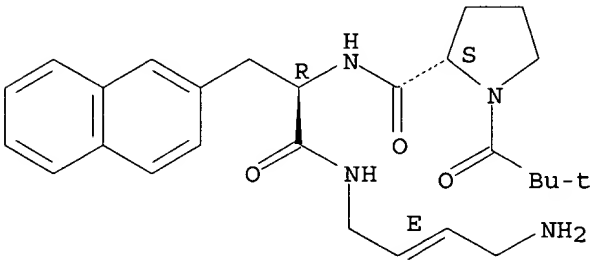
Absolute stereochemistry.
Double bond geometry as shown.



● HCl

RN 289047-98-9 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[(2E)-4-amino-2-butenyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

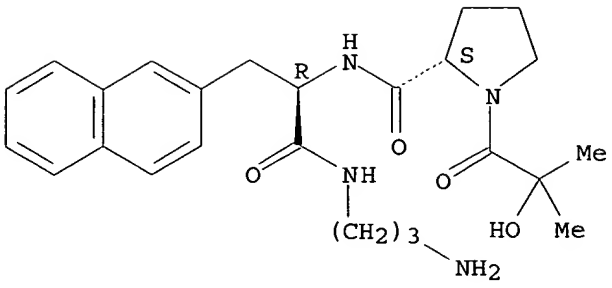
Absolute stereochemistry.
Double bond geometry as shown.



● HCl

RN 289048-00-6 HCAPLUS
CN D-Alaninamide, 2-hydroxy-2-methylpropanoyl-L-prolyl-N-(3-aminopropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

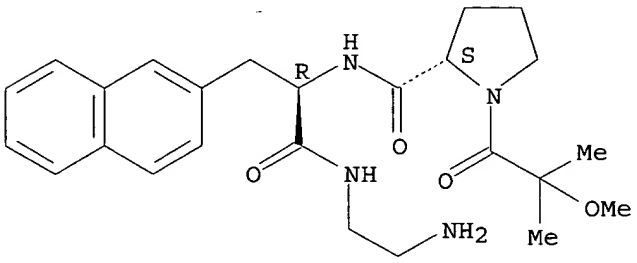
Absolute stereochemistry.



● HCl

RN 289048-01-7 HCAPLUS
CN D-Alaninamide, 1-(2-methoxy-2-methyl-1-oxopropyl)-L-prolyl-N-(2-aminoethyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

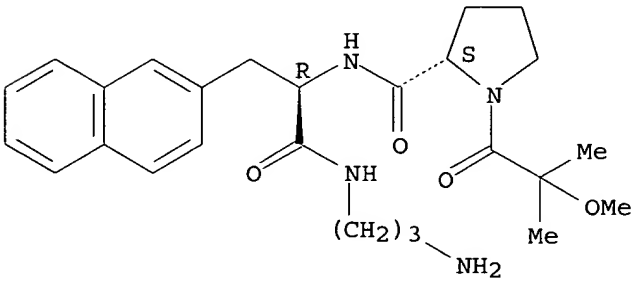
Absolute stereochemistry.



● HCl

RN 289048-02-8 HCAPLUS
CN D-Alaninamide, 1-(2-methoxy-2-methyl-1-oxopropyl)-L-prolyl-N-(3-aminopropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

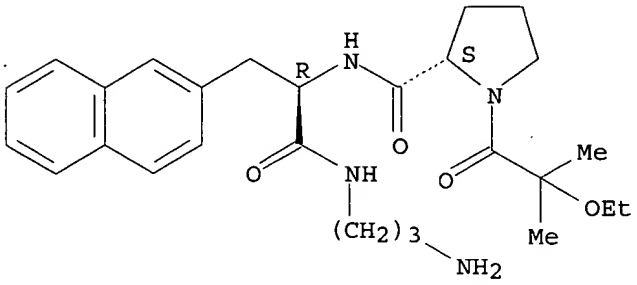
Absolute stereochemistry.



● HCl

RN 289048-03-9 HCAPLUS
CN D-Alaninamide, 1-(2-ethoxy-2-methyl-1-oxopropyl)-L-prolyl-N-(3-aminopropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

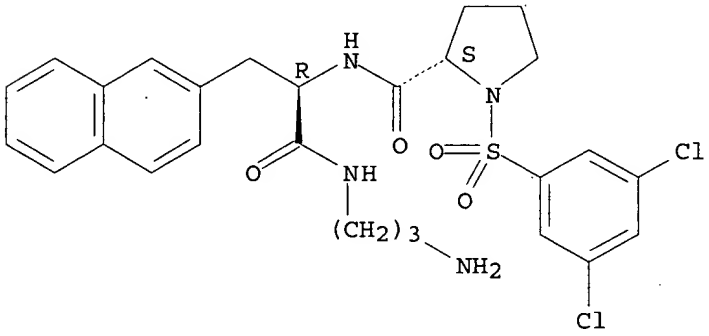
Absolute stereochemistry.



● HCl

RN 289048-04-0 HCAPLUS
CN D-Alaninamide, 1-[(3,5-dichlorophenyl)sulfonyl]-L-prolyl-N-(3-aminopropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

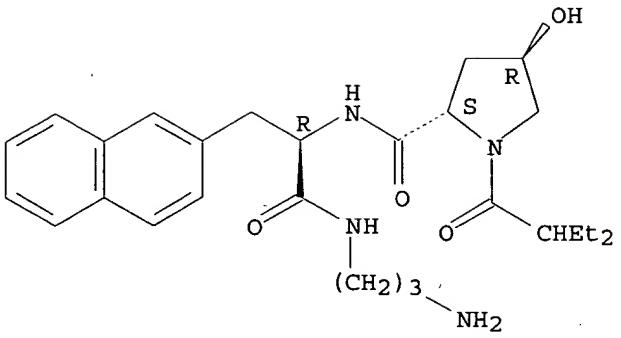
Absolute stereochemistry.



● HCl

RN 289048-05-1 HCAPLUS
CN D-Alaninamide, (4R)-1-(2-ethyl-1-oxobutyl)-4-hydroxy-L-prolyl-N-(3-aminopropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

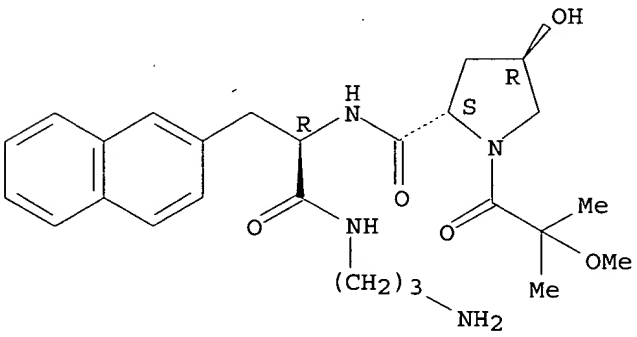
Absolute stereochemistry.



● HCl

RN 289048-06-2 HCAPLUS
CN D-Alaninamide, (4R)-4-hydroxy-1-(2-methoxy-2-methyl-1-oxopropyl)-L-prolyl-N-(3-aminopropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

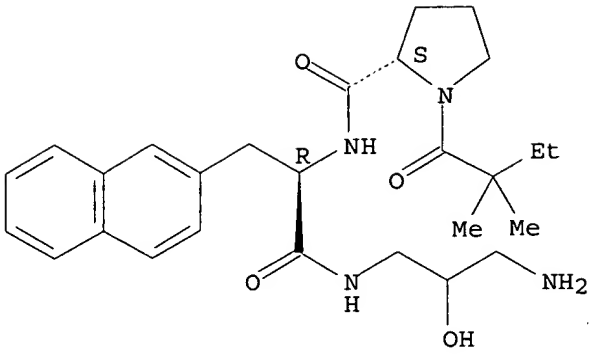
Absolute stereochemistry.



● HCl

RN 289048-07-3 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxobutyl)-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

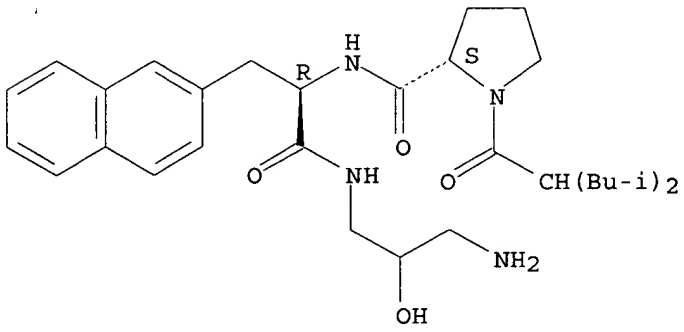
Absolute stereochemistry.



● HCl

RN 289048-08-4 HCAPLUS
CN D-Alaninamide, 1-[4-methyl-2-(2-methylpropyl)-1-oxopentyl]-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

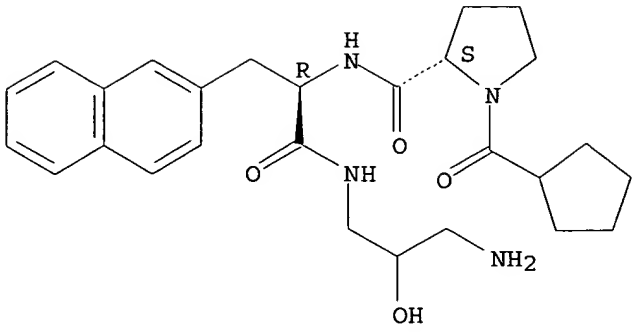
Absolute stereochemistry.



● HCl

RN 289048-09-5 HCAPLUS
CN D-Alaninamide, 1-(cyclopentylcarbonyl)-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

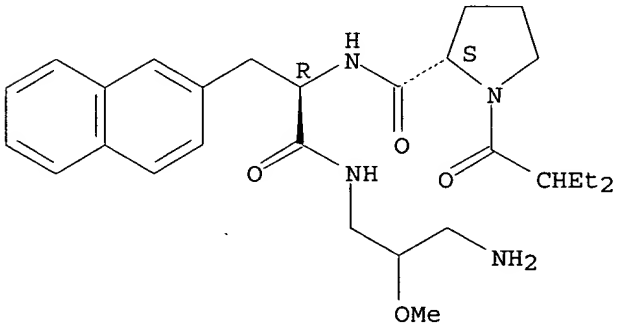
Absolute stereochemistry.



● HCl

RN 289048-10-8 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-(3-amino-2-methoxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

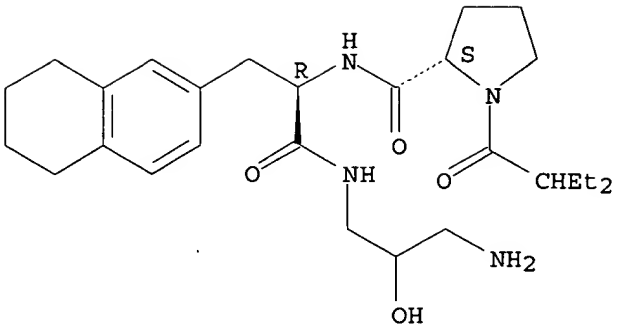
Absolute stereochemistry.



● HCl

RN 289048-11-9 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(5,6,7,8-tetrahydro-2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

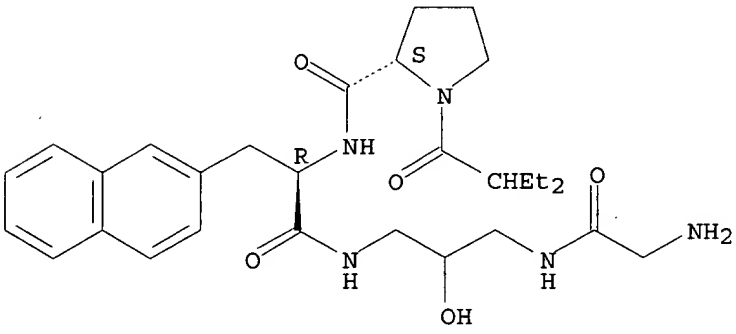
Absolute stereochemistry.



● HCl

RN 289048-12-0 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[3-[(aminoacetyl)amino]-2-hydroxypropyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

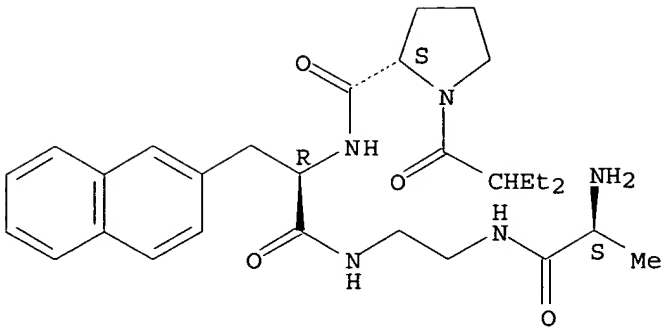
Absolute stereochemistry.



● HCl

RN 289048-13-1 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[2-[[(2S)-2-amino-1-oxopropyl]amino]ethyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

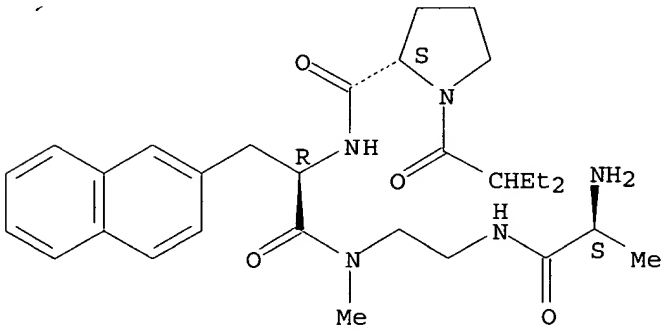
Absolute stereochemistry.



● HCl

RN 289048-14-2 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[2-[[(2S)-2-amino-1-oxopropyl]amino]ethyl]-N-methyl-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

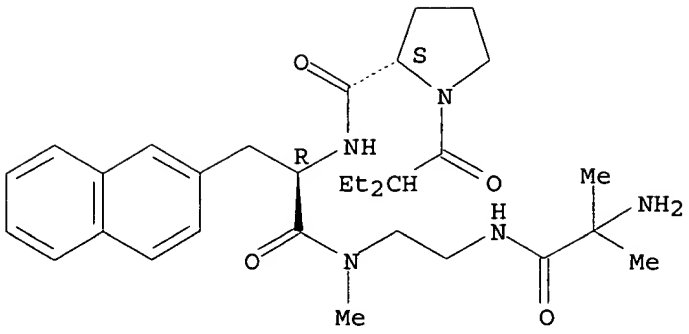
Absolute stereochemistry.



● HCl

RN 289048-15-3 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[2-[(2-amino-2-methyl-1-oxopropyl)amino]ethyl]-N-methyl-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

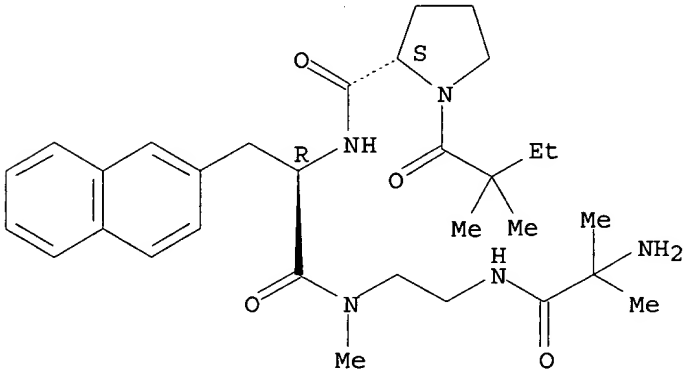
Absolute stereochemistry.



● HCl

RN 289048-16-4 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxobutyl)-L-prolyl-N-[2-[(2-amino-2-methyl-1-oxopropyl)amino]ethyl]-N-methyl-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

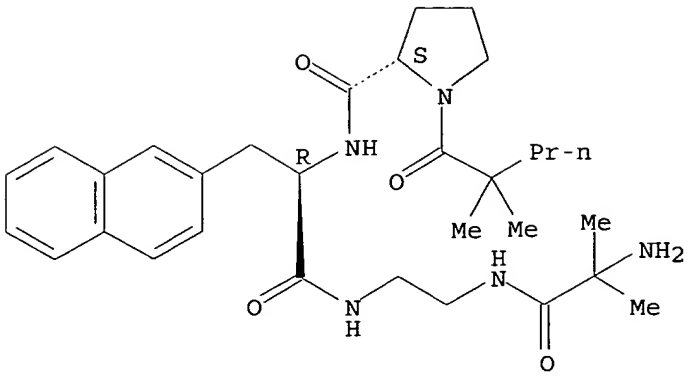
Absolute stereochemistry.



● HCl

RN 289048-17-5 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopentyl)-L-prolyl-N-[2-[(2-amino-2-methyl-1-oxopropyl)amino]ethyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

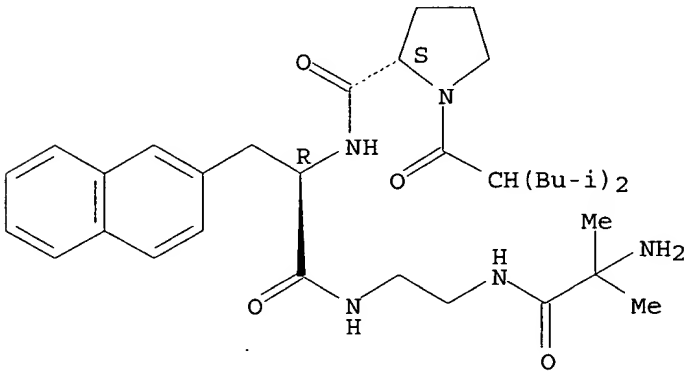
Absolute stereochemistry.



● HCl

RN 289048-18-6 HCAPLUS
CN D-Alaninamide, 1-[4-methyl-2-(2-methylpropyl)-1-oxopentyl]-L-prolyl-N-[2-[(2-amino-2-methyl-1-oxopropyl)amino]ethyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

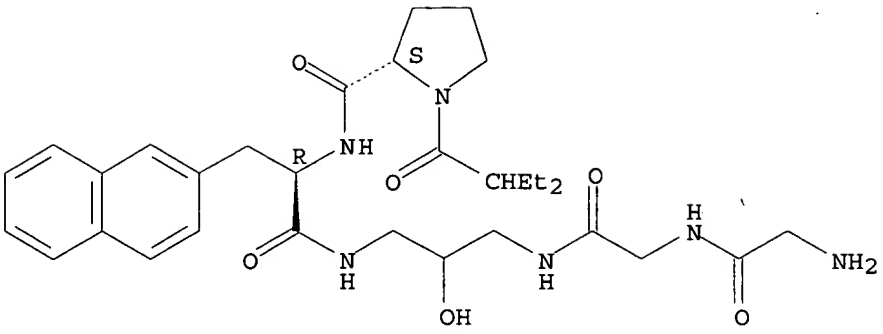
Absolute stereochemistry.



● HCl

RN 289048-19-7 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[3-[(glycylglycyl)amino]-2-hydroxypropyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

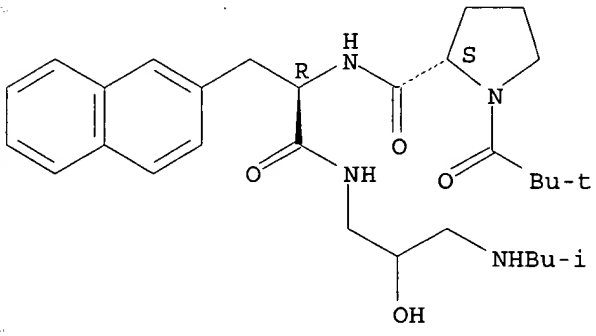
Absolute stereochemistry.



● HCl

RN 289048-20-0 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[2-hydroxy-3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

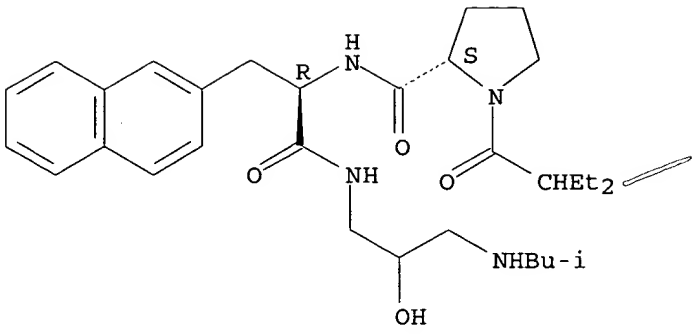
Absolute stereochemistry.



● HCl

RN 289048-21-1 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[2-hydroxy-3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

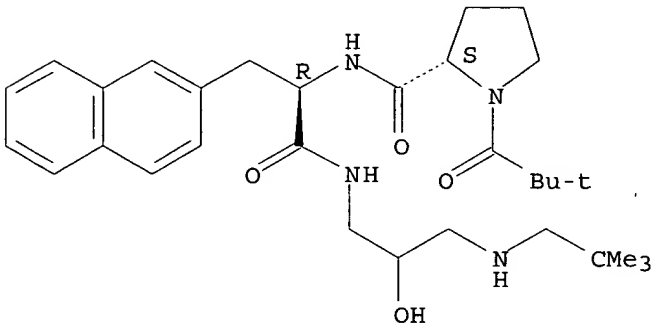
Absolute stereochemistry.



● HCl

RN 289048-22-2 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[(2,2-dimethylpropyl)amino]-2-hydroxypropyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

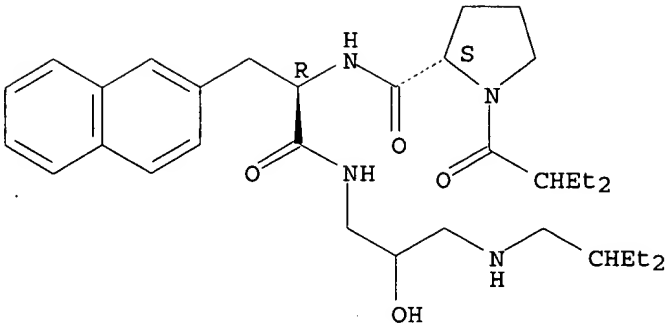
Absolute stereochemistry.



● HCl

RN 289048-23-3 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[3-[(2-ethylbutyl)amino]-2-hydroxypropyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

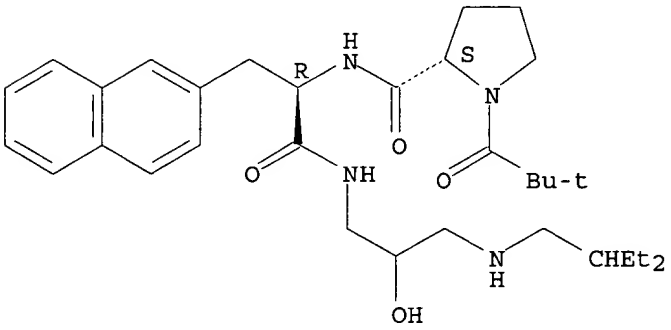
Absolute stereochemistry.



● HCl

RN 289048-25-5 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[(2-ethylbutyl)amino]-2-hydroxypropyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

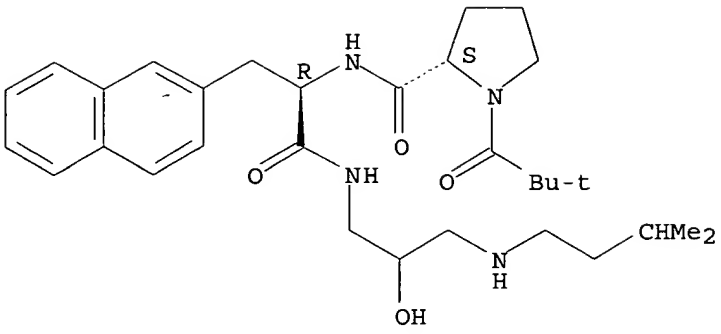
Absolute stereochemistry.



● HCl

RN 289048-26-6 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[2-hydroxy-3-[(3-methylbutyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

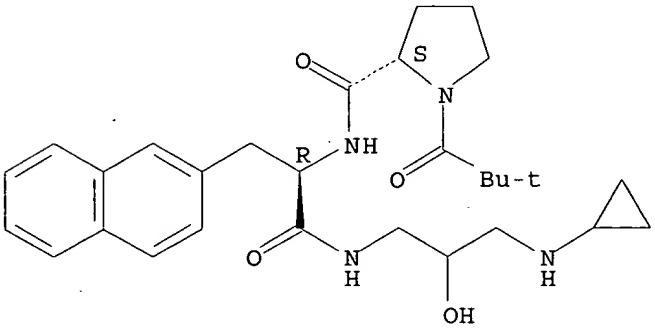
Absolute stereochemistry.



● HCl

RN 289048-27-7 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-(cyclopropylamino)-2-hydroxypropyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

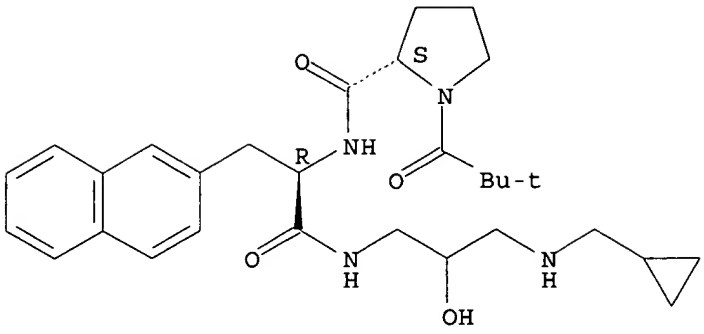
Absolute stereochemistry.



● HCl

RN 289048-28-8 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[(cyclopropylmethyl)amino]-2-hydroxypropyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

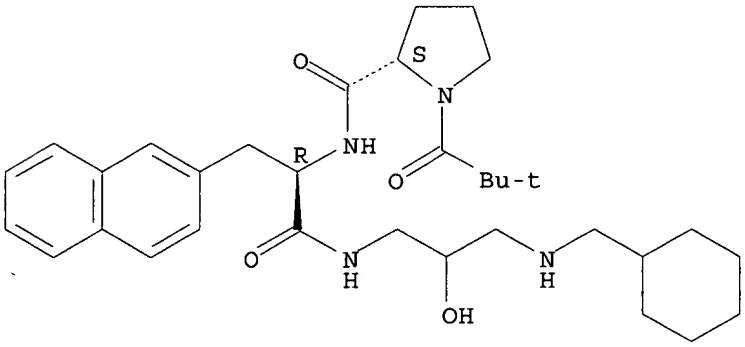
Absolute stereochemistry.



● HCl

RN 289048-29-9 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[(cyclohexylmethyl)amino]-2-hydroxypropyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

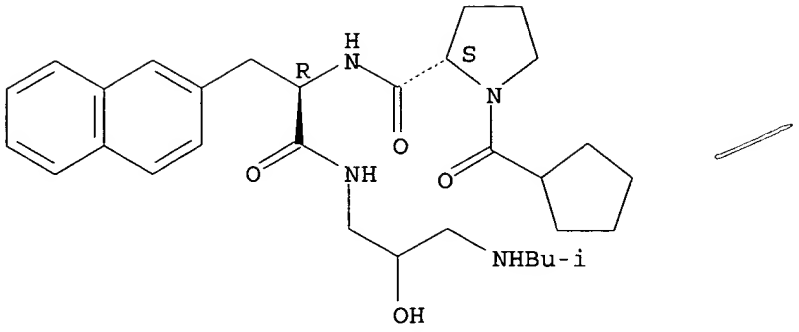
Absolute stereochemistry.



● HCl

RN 289048-30-2 HCAPLUS
CN D-Alaninamide, 1-(cyclopentylcarbonyl)-L-prolyl-N-[2-hydroxy-3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

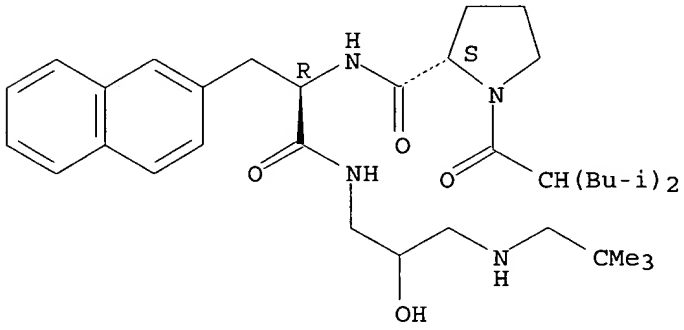
Absolute stereochemistry.



● HCl

RN 289048-31-3 HCAPLUS
CN D-Alaninamide, 1-[4-methyl-2-(2-methylpropyl)-1-oxopentyl]-L-prolyl-N-[3-[(2,2-dimethylpropyl)amino]-2-hydroxypropyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

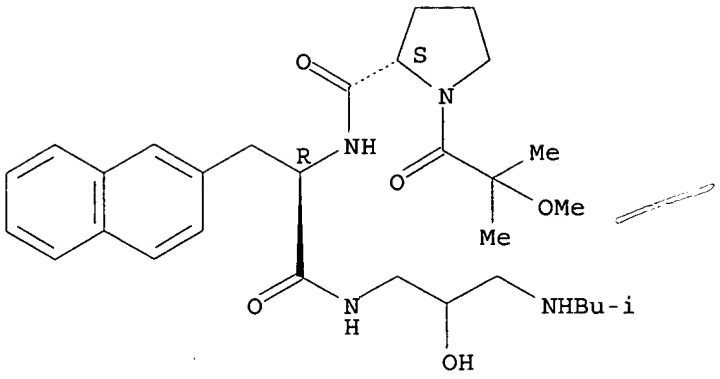
Absolute stereochemistry.



● HCl

RN 289048-32-4 HCAPLUS
CN D-Alaninamide, 1-(2-methoxy-2-methyl-1-oxopropyl)-L-prolyl-N-[2-hydroxy-3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

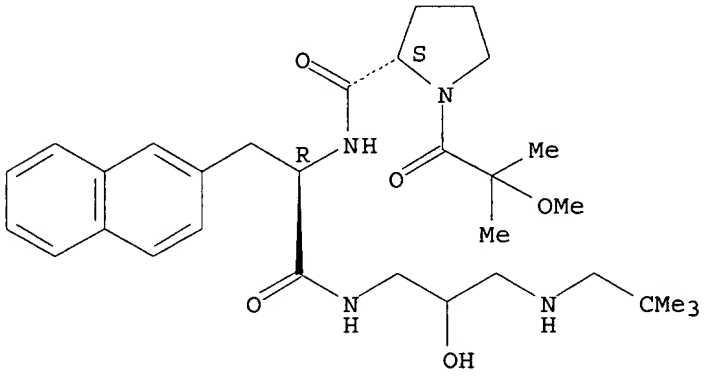
Absolute stereochemistry.



● HCl

RN 289048-33-5 HCAPLUS
CN D-Alaninamide, 1-(2-methoxy-2-methyl-1-oxopropyl)-L-prolyl-N-[3-[(2,2-dimethylpropyl)amino]-2-hydroxypropyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

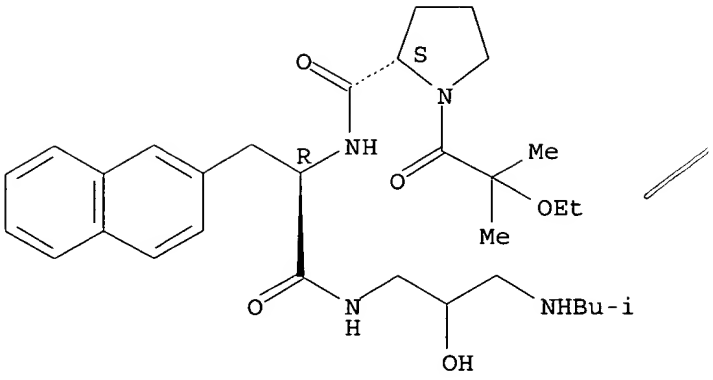
Absolute stereochemistry.



● HCl

RN 289048-34-6 HCAPLUS
CN D-Alaninamide, 1-(2-ethoxy-2-methyl-1-oxopropyl)-L-prolyl-N-[2-hydroxy-3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

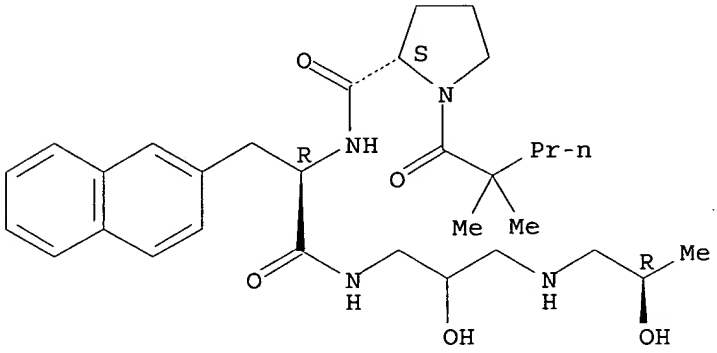
Absolute stereochemistry.



● HCl

RN 289048-35-7 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopentyl)-L-prolyl-N-[2-hydroxy-3-[[(2R)-2-hydroxypropyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

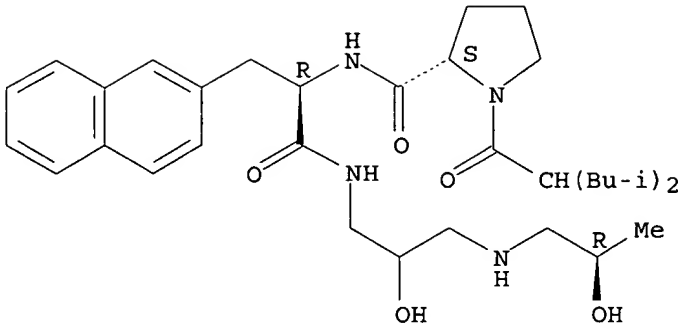
Absolute stereochemistry.



● HCl

RN 289048-36-8 HCAPLUS
CN D-Alaninamide, 1-[4-methyl-2-(2-methylpropyl)-1-oxopentyl]-L-prolyl-N-[2-hydroxy-3-[[(2R)-2-hydroxypropyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

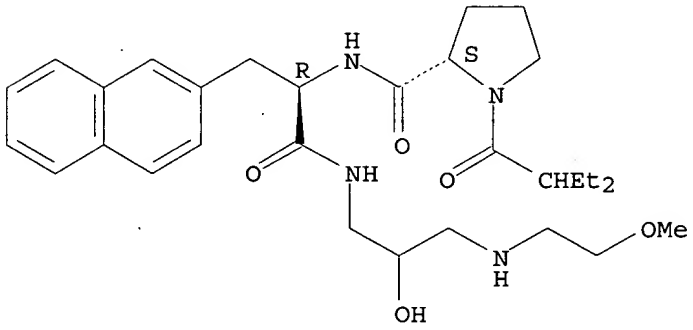
Absolute stereochemistry.



● HCl

RN 289048-37-9 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[2-hydroxy-3-[(2-methoxyethyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

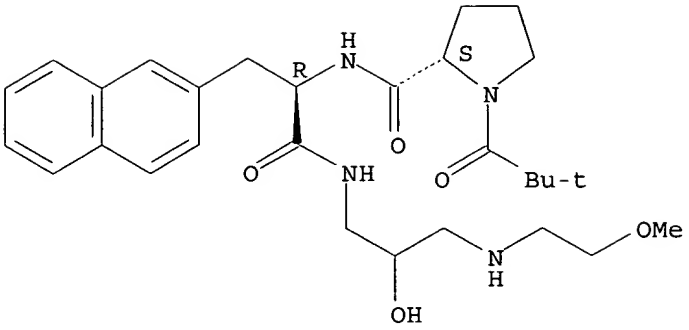
Absolute stereochemistry.



● HCl

RN 289048-38-0 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[2-hydroxy-3-[(2-methoxyethyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

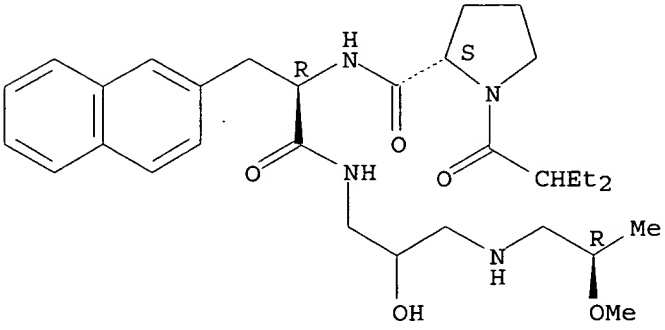
Absolute stereochemistry.



● HCl

RN 289048-39-1 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[2-hydroxy-3-[[(2R)-2-methoxypropyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

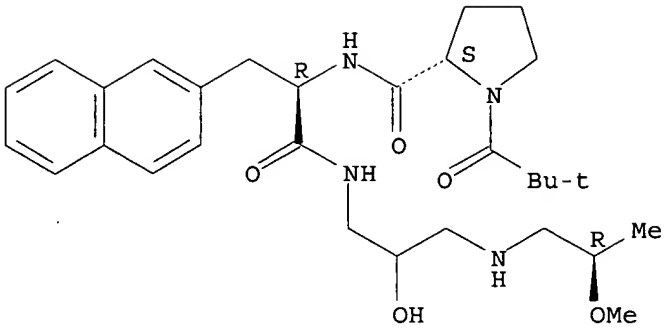
Absolute stereochemistry.



● HCl

RN 289048-40-4 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[2-hydroxy-3-[[(2R)-2-methoxypropyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

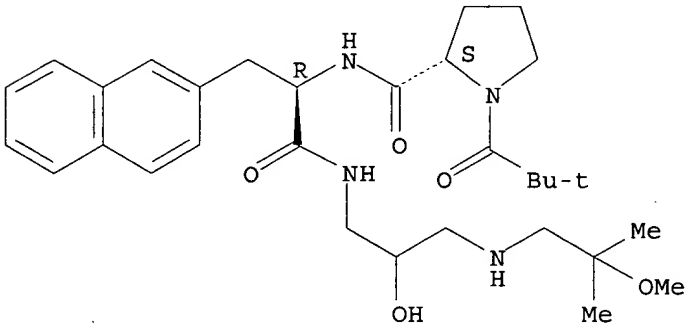
Absolute stereochemistry.



● HCl

RN 289048-41-5 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[2-hydroxy-3-[(2-methoxy-2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

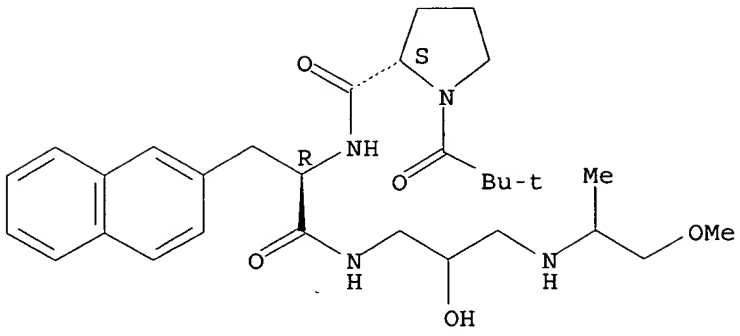
Absolute stereochemistry.



● HCl

RN 289048-42-6 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[2-hydroxy-3-[(2-methoxy-1-methylethyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

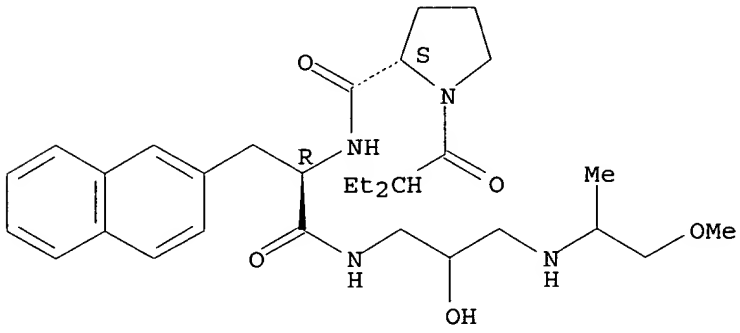
Absolute stereochemistry.



● HCl

RN 289048-43-7 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[2-hydroxy-3-[(2-methoxy-1-methylethyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

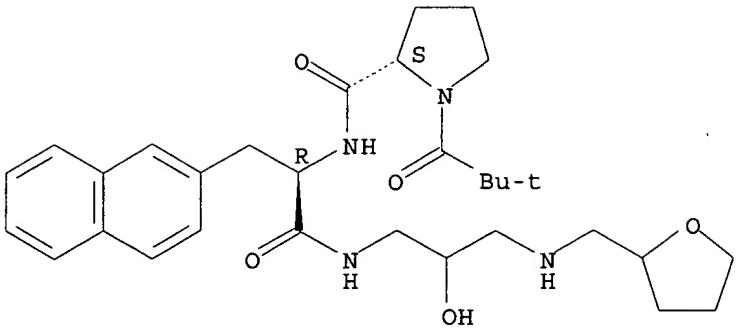
Absolute stereochemistry.



● HCl

RN 289048-44-8 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[2-hydroxy-3-[[(tetrahydro-2-furanyl)methyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

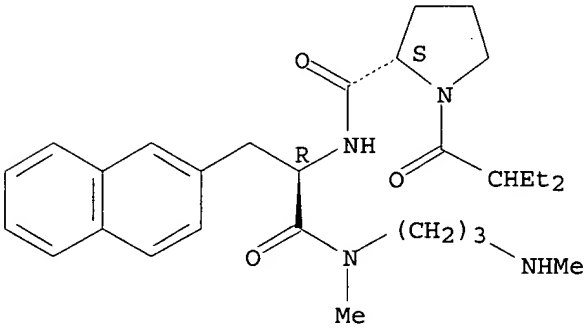
Absolute stereochemistry.



● HCl

RN 289048-45-9 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-methyl-N-[3-(methylamino)propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

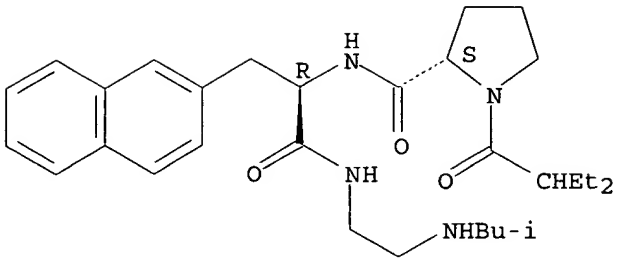
Absolute stereochemistry.



● HCl

RN 289048-46-0 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[2-[(2-methylpropyl)amino]ethyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

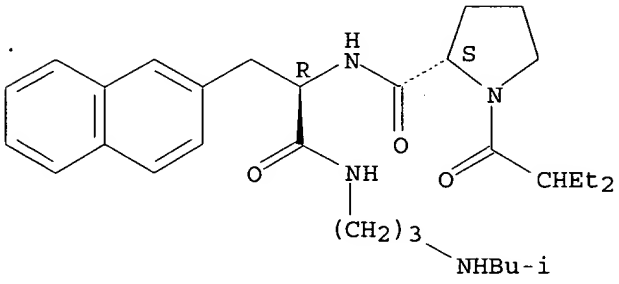
Absolute stereochemistry.



● HCl

RN 289048-47-1 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

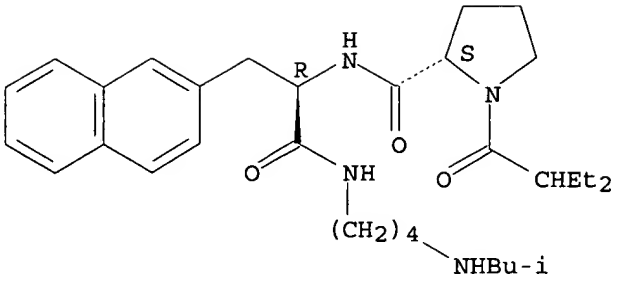
Absolute stereochemistry.



● HCl

RN 289048-48-2 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[4-[(2-methylpropyl)amino]butyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

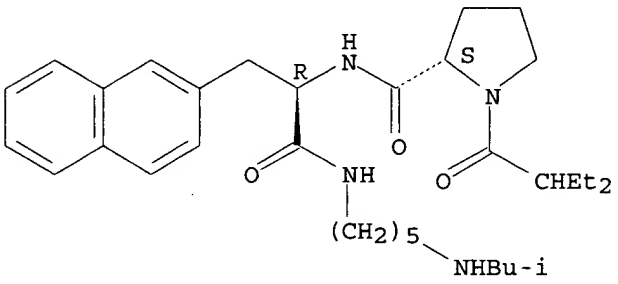
Absolute stereochemistry.



● HCl

RN 289048-49-3 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[5-[(2-methylpropyl)amino]pentyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

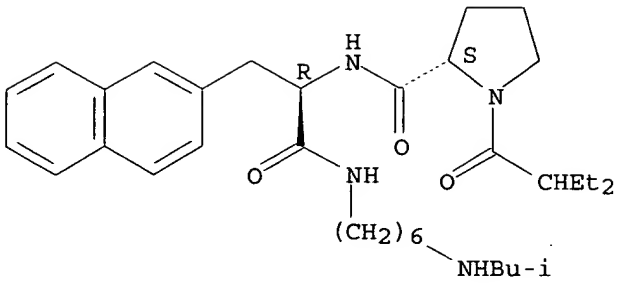
Absolute stereochemistry.



● HCl

RN 289048-50-6 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[6-[(2-methylpropyl)amino]hexyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

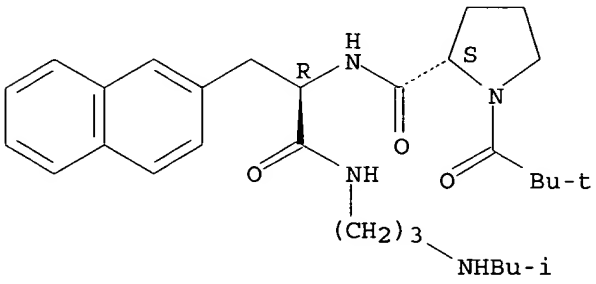
Absolute stereochemistry.



● HCl

RN 289048-51-7 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

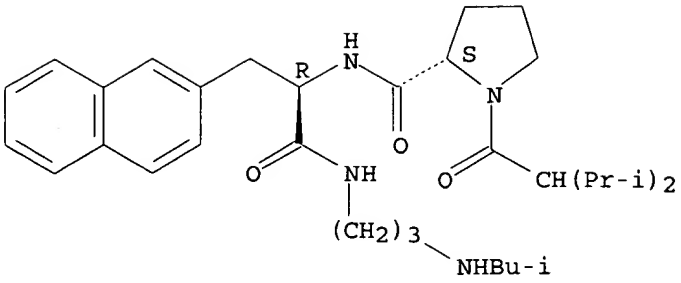
Absolute stereochemistry.



● HCl

RN 289048-52-8 HCAPLUS
CN D-Alaninamide, 1-[3-methyl-2-(1-methylethyl)-1-oxobutyl]-L-prolyl-N-[3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

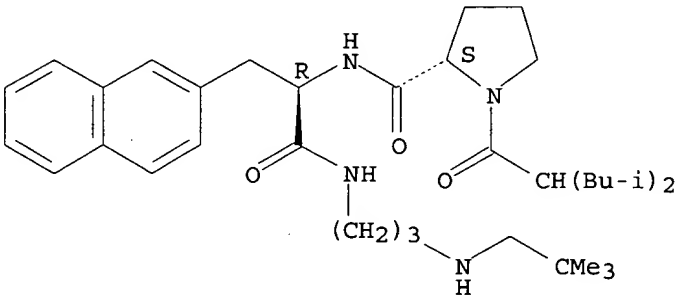
Absolute stereochemistry.



● HCl

RN 289048-53-9 HCAPLUS
CN D-Alaninamide, 1-[4-methyl-2-(2-methylpropyl)-1-oxopentyl]-L-prolyl-N-[3-[(2,2-dimethylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

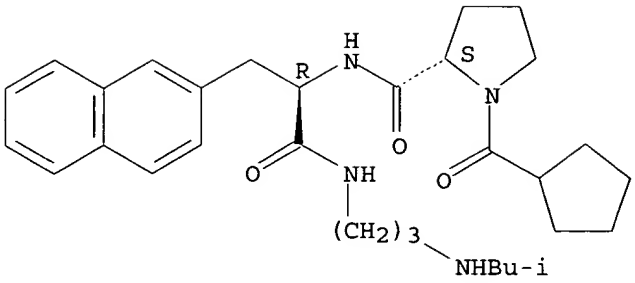
Absolute stereochemistry.



● HCl

RN 289048-54-0 HCAPLUS
CN D-Alaninamide, 1-(cyclopentylcarbonyl)-L-prolyl-N-[3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

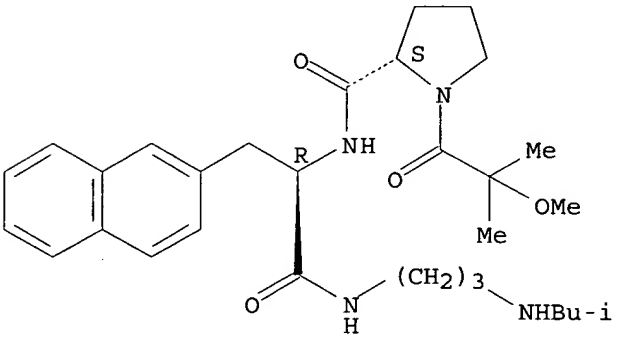
Absolute stereochemistry.



● HCl

RN 289048-55-1 HCAPLUS
CN D-Alaninamide, 1-(2-methoxy-2-methyl-1-oxopropyl)-L-prolyl-N-[3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

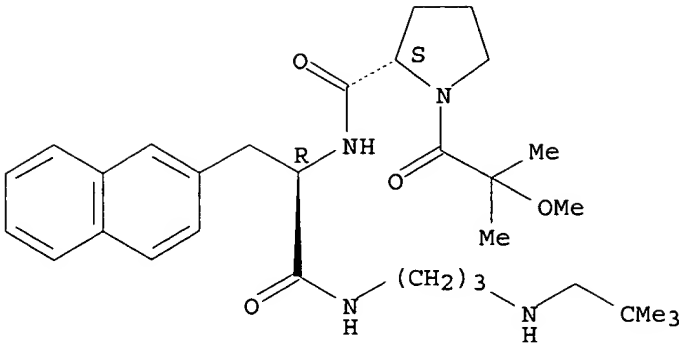
Absolute stereochemistry.



● HCl

RN 289048-56-2 HCAPLUS
CN D-Alaninamide, 1-(2-methoxy-2-methyl-1-oxopropyl)-L-prolyl-N-[3-[(2,2-dimethylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

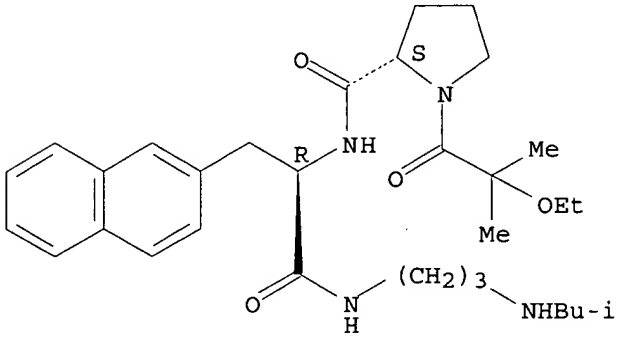
Absolute stereochemistry.



● HCl

RN 289048-57-3 HCAPLUS
CN D-Alaninamide, 1-(2-ethoxy-2-methyl-1-oxopropyl)-L-prolyl-N-[3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

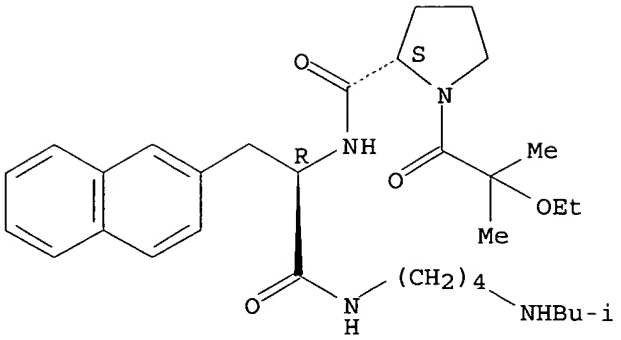
Absolute stereochemistry.



● HCl

RN 289048-58-4 HCAPLUS
CN D-Alaninamide, 1-(2-ethoxy-2-methyl-1-oxopropyl)-L-prolyl-N-[4-[(2-methylpropyl)amino]butyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

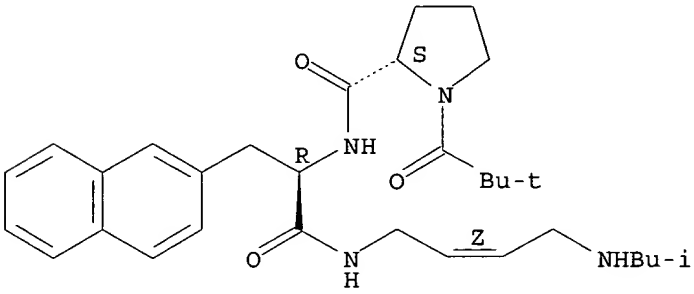
Absolute stereochemistry.



● HCl

RN 289048-59-5 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[(2Z)-4-[(2-methylpropyl)amino]-2-butenyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

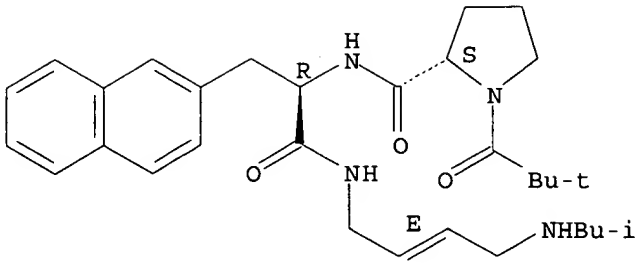
Absolute stereochemistry.
Double bond geometry as shown.



● HCl

RN 289048-60-8 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[(2E)-4-[(2-methylpropyl)amino]-2-butenyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

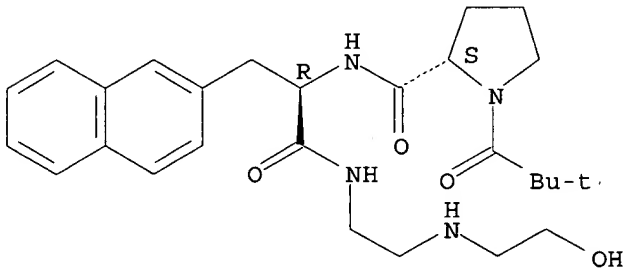
Absolute stereochemistry.
Double bond geometry as shown.



● HCl

RN 289048-61-9 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[2-[(2-hydroxyethyl)amino]ethyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

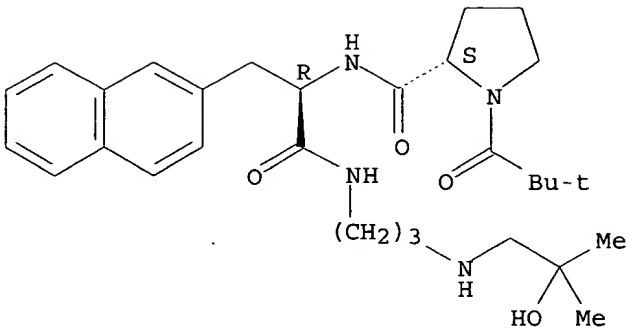
Absolute stereochemistry.



● HCl

RN 289048-62-0 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[(2-hydroxy-2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

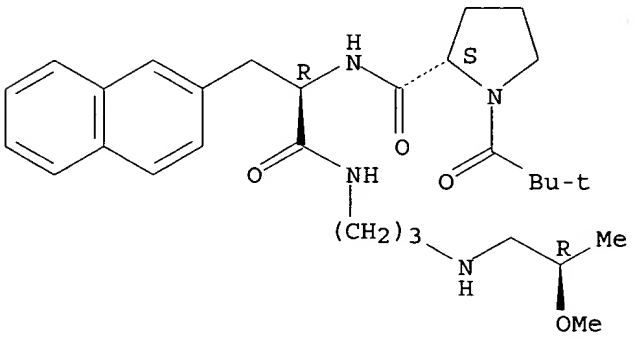
Absolute stereochemistry.



● HCl

RN 289048-63-1 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[[(2R)-2-methoxypropyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

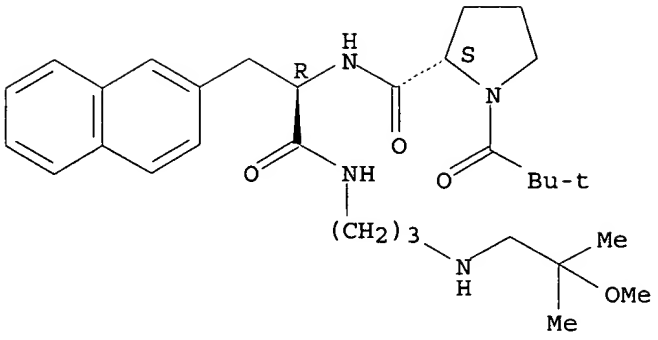
Absolute stereochemistry.



● HCl

RN 289048-64-2 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[(2-methoxy-2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

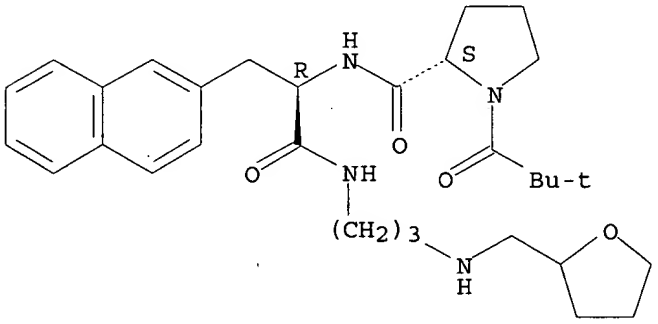
Absolute stereochemistry.



● HCl

RN 289048-65-3 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-3-(2-naphthalenyl)-N-[3-[[(tetrahydro-2-furanyl)methyl]amino]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

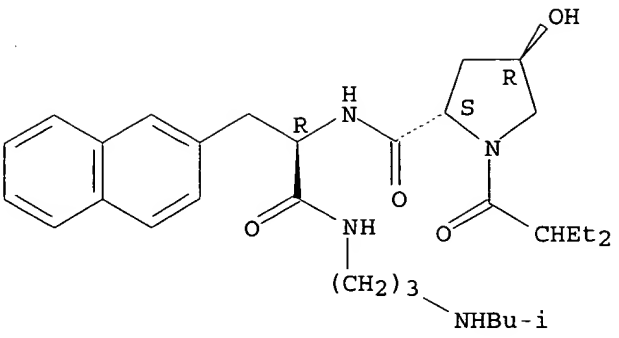
Absolute stereochemistry.



● HCl

RN 289048-66-4 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-4-hydroxy-L-prolyl-N-[3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

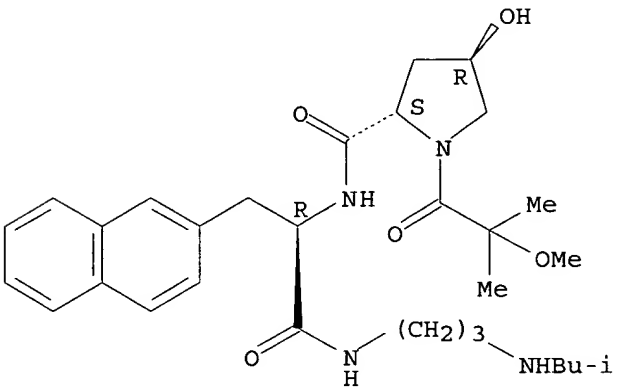
Absolute stereochemistry.



● HCl

RN 289048-67-5 HCAPLUS
CN D-Alaninamide, (4R)-4-hydroxy-1-(2-methoxy-2-methyl-1-oxopropyl)-L-prolyl-N-[3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

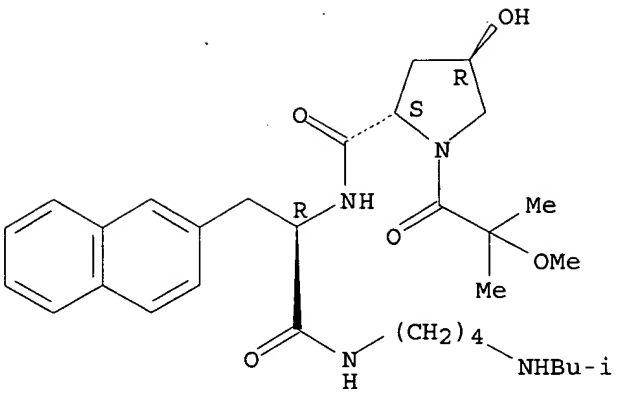
Absolute stereochemistry.



● HCl

RN 289048-68-6 HCAPLUS
CN D-Alaninamide, (4R)-4-hydroxy-1-(2-methoxy-2-methyl-1-oxopropyl)-L-prolyl-N-[4-[(2-methylpropyl)amino]butyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

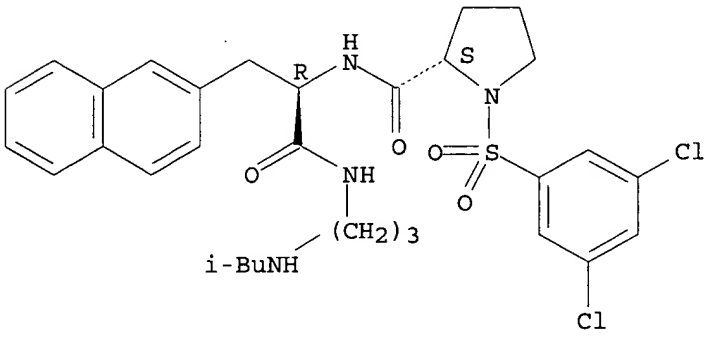
Absolute stereochemistry.



● HCl

RN 289048-69-7 HCAPLUS
CN D-Alaninamide, 1-[(3,5-dichlorophenyl)sulfonyl]-L-prolyl-N-[3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

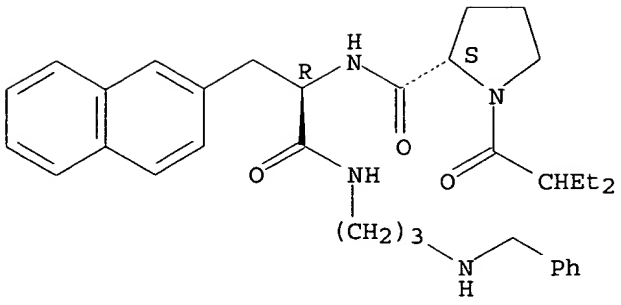
Absolute stereochemistry.



● HCl

RN 289048-70-0 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-3-(2-naphthalenyl)-N-[3-[(phenylmethyl)amino]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

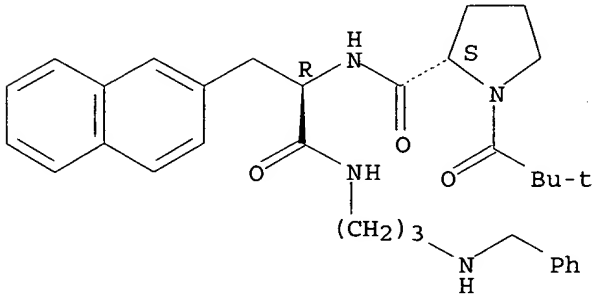
Absolute stereochemistry.



● HCl

RN 289048-71-1 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-3-(2-naphthalenyl)-N-[3-[(phenylmethyl)amino]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

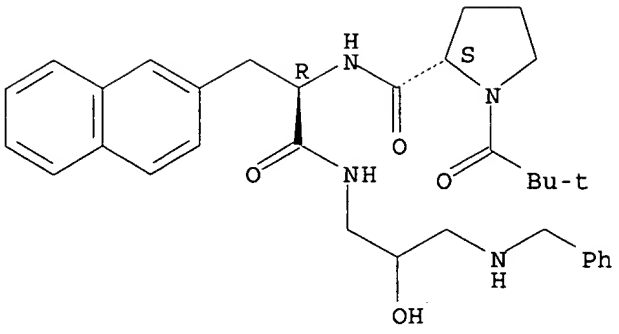
Absolute stereochemistry.



● HCl

RN 289048-72-2 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[2-hydroxy-3-[(phenylmethyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

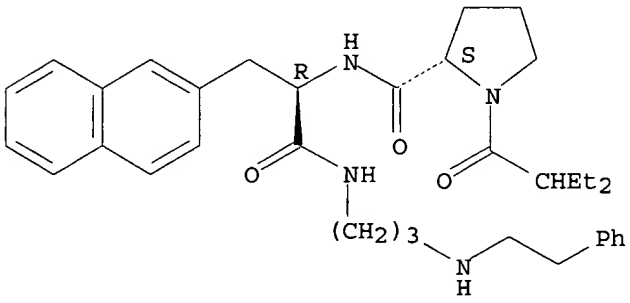
Absolute stereochemistry.



● HCl

RN 289048-73-3 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-3-(2-naphthalenyl)-N-[3-[(2-phenylethyl)amino]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

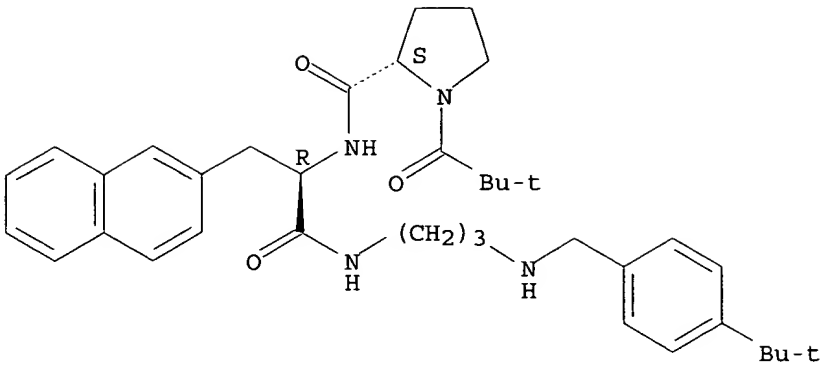
Absolute stereochemistry.



● HCl

RN 289048-74-4 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[[[4-(1,1-dimethylethyl)phenyl]methyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

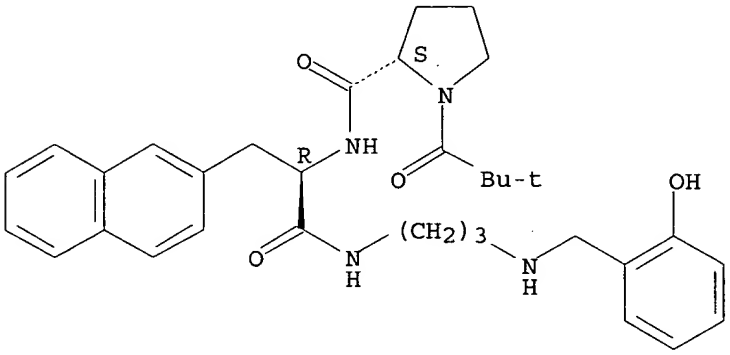
Absolute stereochemistry.



● HCl

RN 289048-75-5 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[[(2-hydroxyphenyl)methyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

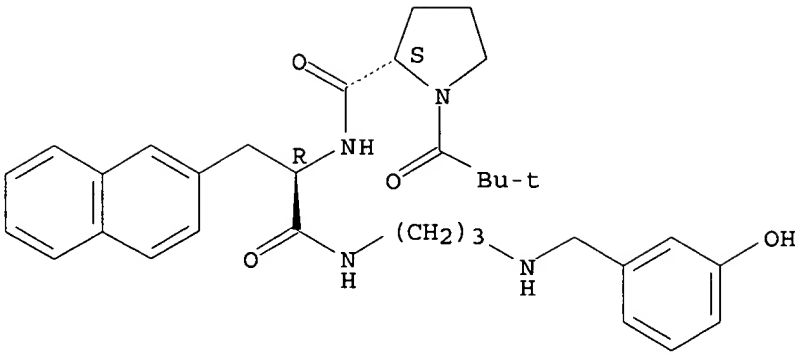
Absolute stereochemistry.



● HCl

RN 289048-76-6 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[[(3-hydroxyphenyl)methyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

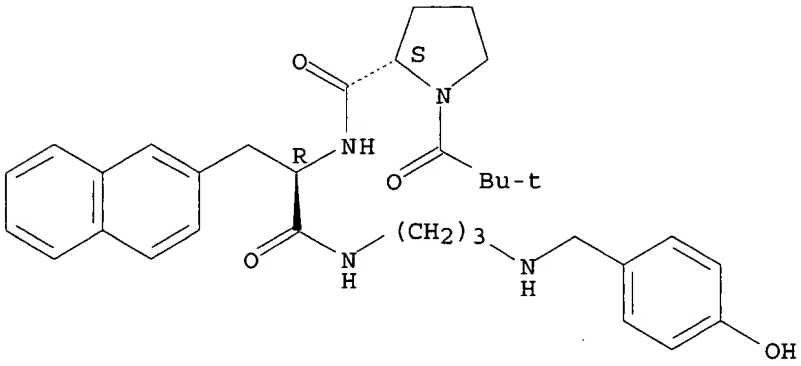
Absolute stereochemistry.



● HCl

RN 289048-77-7 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[[(4-hydroxyphenyl)methyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

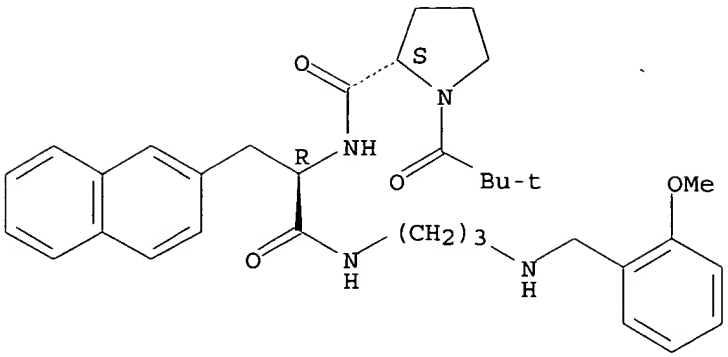
Absolute stereochemistry.



● HCl

RN 289048-78-8 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[[(2-methoxyphenyl)methyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

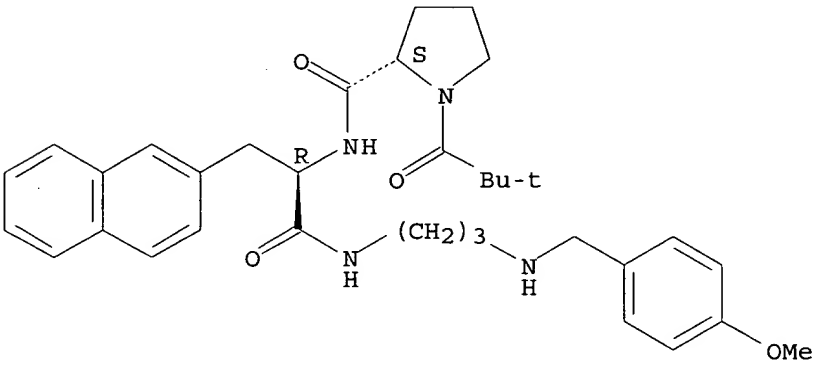
Absolute stereochemistry.



● HCl

RN 289048-79-9 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[[(4-methoxyphenyl)methyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

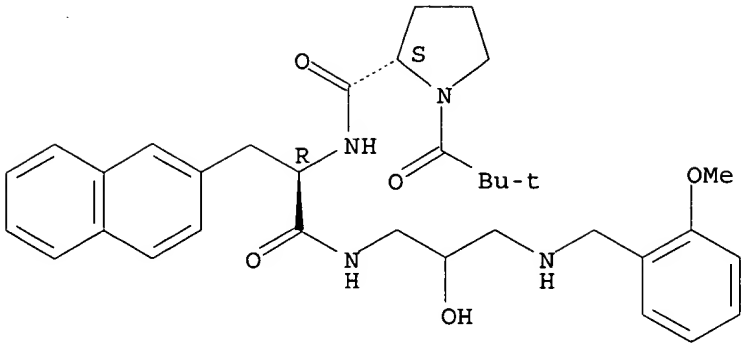
Absolute stereochemistry.



● HCl

RN 289048-80-2 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[2-hydroxy-3-[[(2-methoxyphenyl)methyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

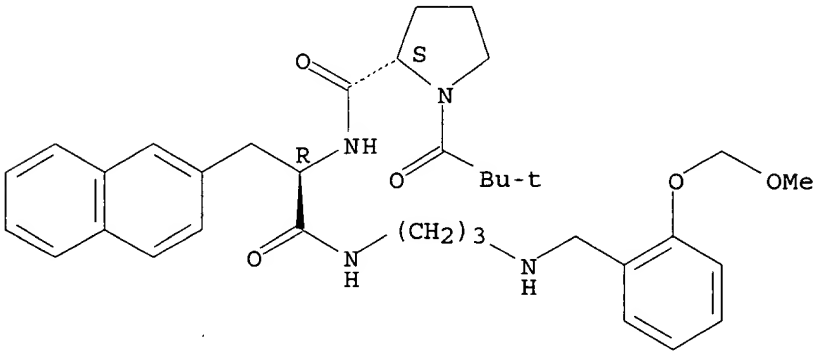
Absolute stereochemistry.



● HCl

RN 289048-81-3 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[[[2-(methoxymethoxy)phenyl]methyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

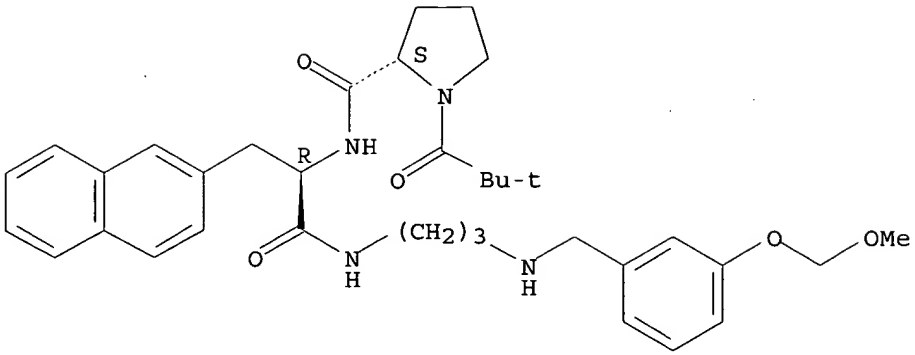
Absolute stereochemistry.



● HCl

RN 289048-82-4 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[[[3-(methoxymethoxy)phenyl]methyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

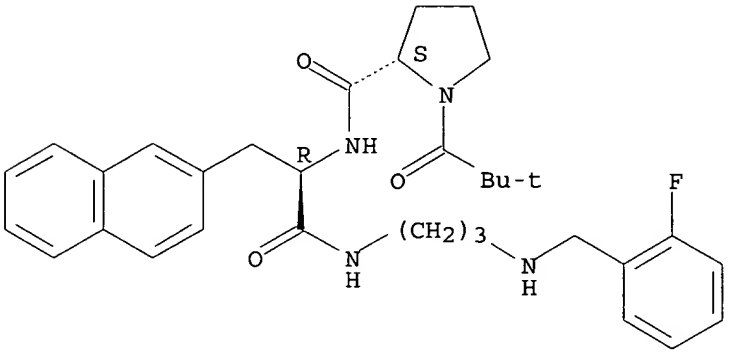
Absolute stereochemistry.



● HCl

RN 289048-83-5 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[[(2-fluorophenyl)methyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

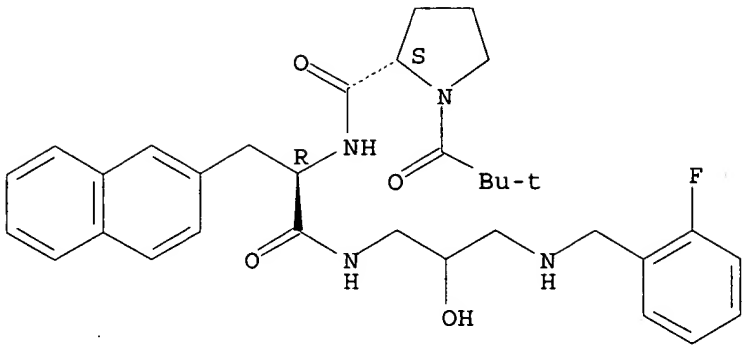
Absolute stereochemistry.



● HCl

RN 289048-84-6 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[[(2-fluorophenyl)methyl]amino]-2-hydroxypropyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

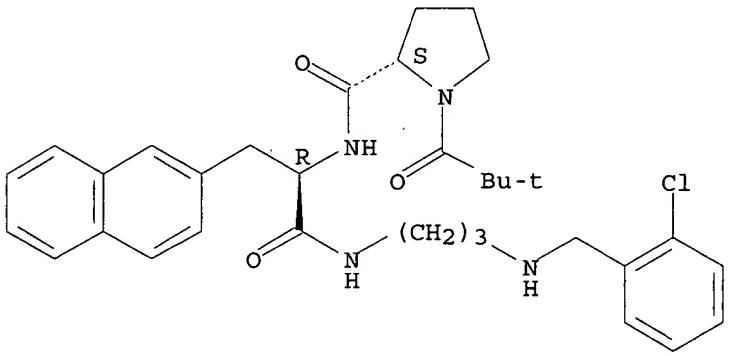
Absolute stereochemistry.



● HCl

RN 289048-85-7 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[[(2-chlorophenyl)methyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

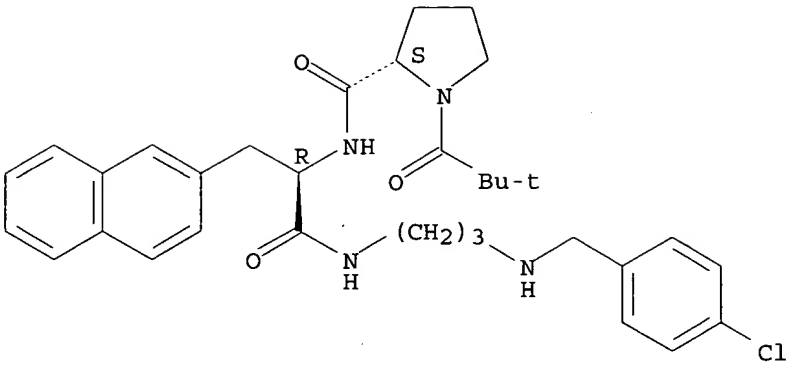
Absolute stereochemistry.



● HCl

RN 289048-86-8 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[[(4-chlorophenyl)methyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

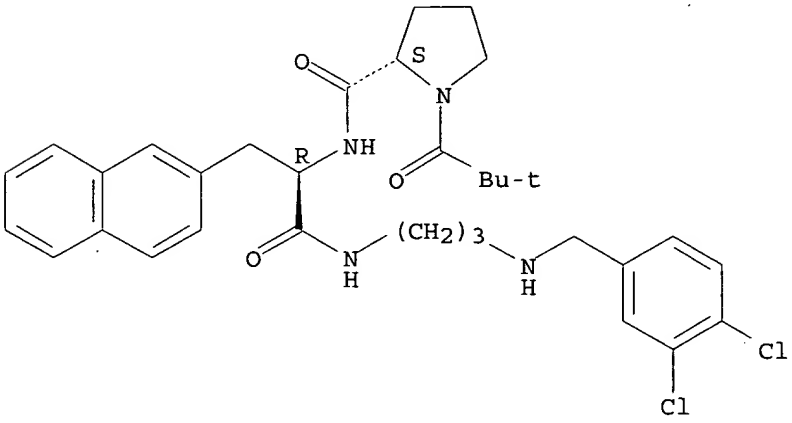
Absolute stereochemistry.



● HCl

RN 289048-87-9 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[[(3,4-dichlorophenyl)methyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

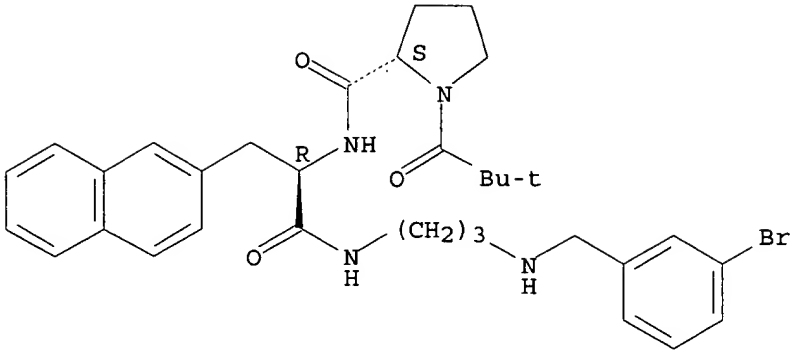
Absolute stereochemistry.



● HCl

RN 289048-88-0 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[[(3-bromophenyl)methyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

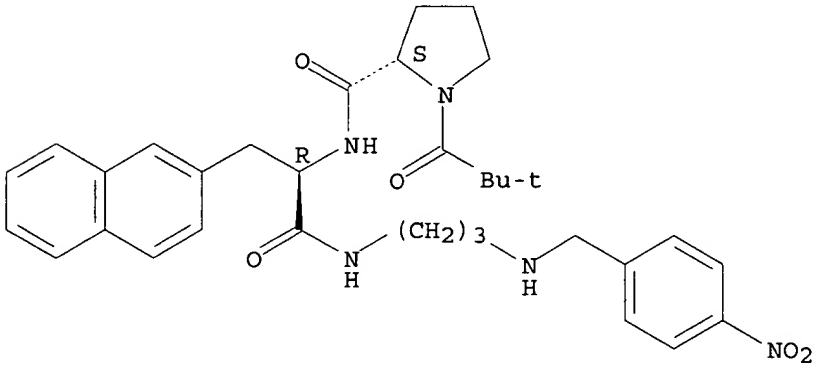
Absolute stereochemistry.



● HCl

RN 289048-89-1 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-3-(2-naphthalenyl)-N-[3-[[(4-nitrophenyl)methyl]amino]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

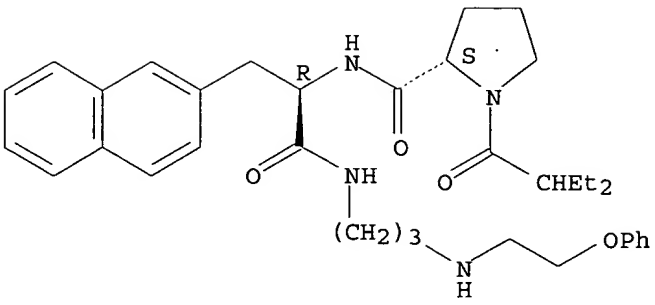
Absolute stereochemistry.



● HCl

RN 289048-90-4 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-3-(2-naphthalenyl)-N-[3-[(2-phenoxyethyl)amino]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

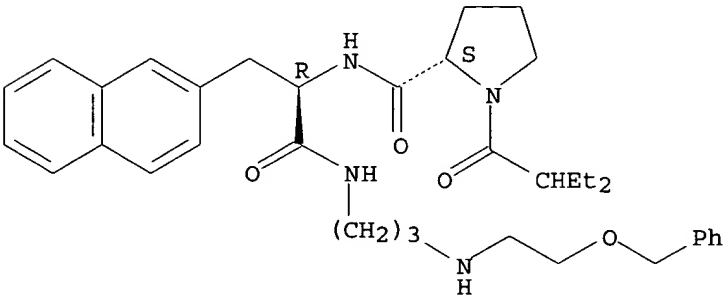
Absolute stereochemistry.



● HCl

RN 289048-91-5 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-3-(2-naphthalenyl)-N-[3-[[2-(phenylmethoxy)ethyl]amino]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

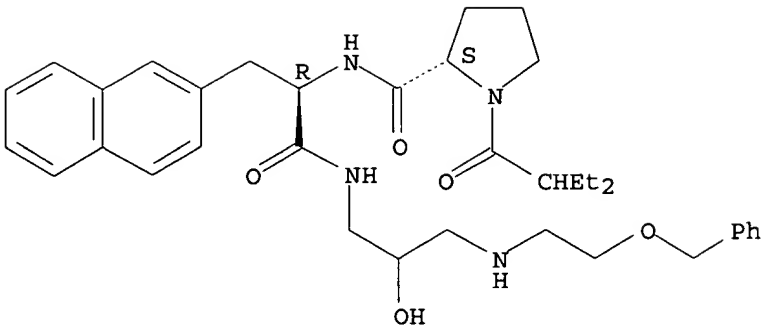
Absolute stereochemistry.



● HCl

RN 289048-92-6 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[2-hydroxy-3-[[2-(phenylmethoxy)ethyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

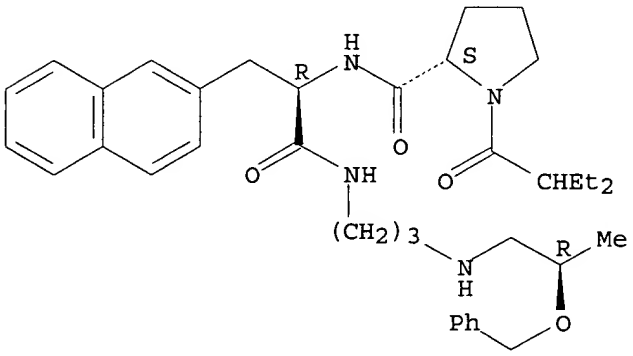
Absolute stereochemistry.



● HCl

RN 289048-93-7 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-3-(2-naphthalenyl)-N-[3-[[(2R)-2-(phenylmethoxy)propyl]amino]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

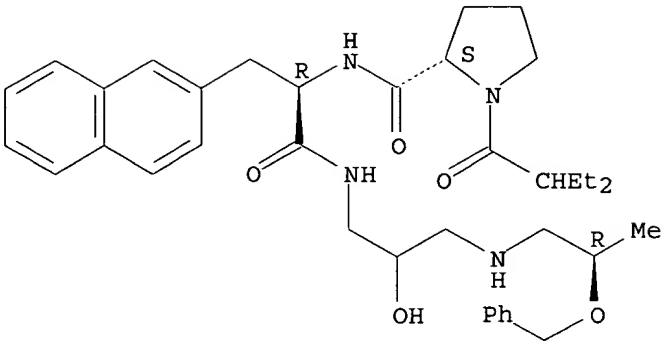
Absolute stereochemistry.



● HCl

RN 289048-94-8 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[2-hydroxy-3-[[(2R)-2-(phenylmethoxy)propyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

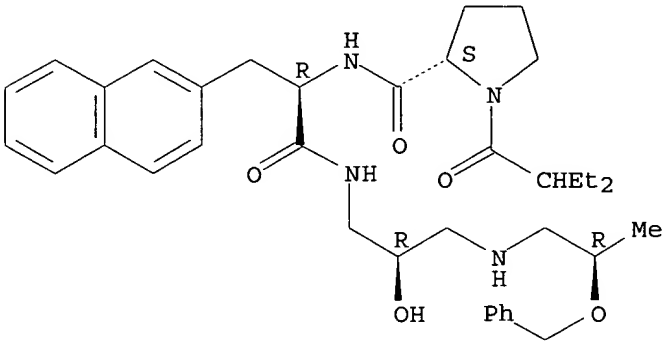
Absolute stereochemistry.



● HCl

RN 289048-95-9 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[(2R)-2-hydroxy-3-[[(2R)-2-(phenylmethoxy)propyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

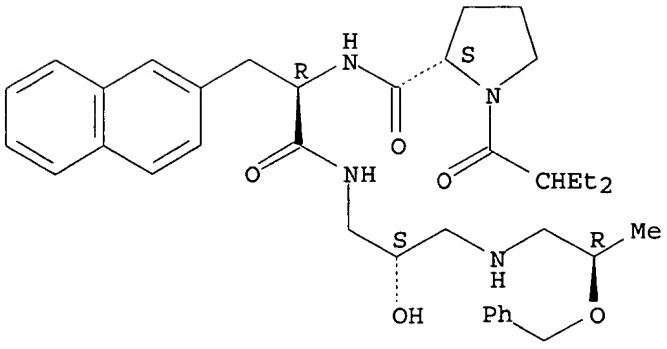
Absolute stereochemistry.



● HCl

RN 289048-96-0 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[(2S)-2-hydroxy-3-[[(2R)-2-(phenylmethoxy)propyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

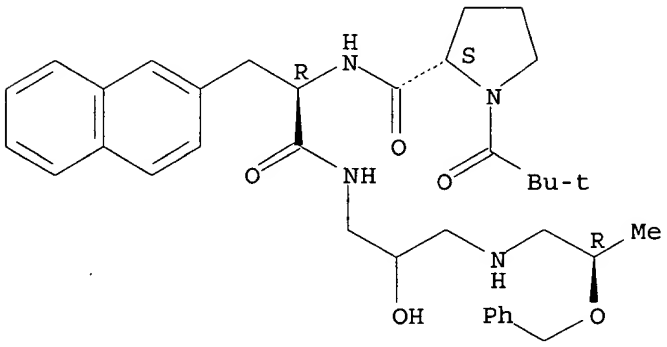
Absolute stereochemistry.



● HCl

RN 289048-97-1 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[2-hydroxy-3-[[(2R)-2-(phenylmethoxy)propyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

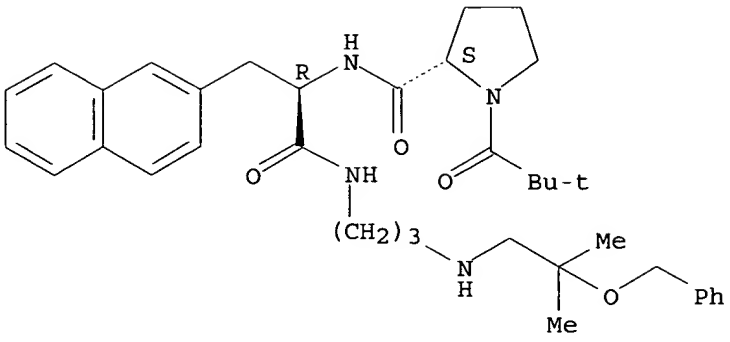
Absolute stereochemistry.



● HCl

RN 289048-98-2 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[[2-methyl-2-(phenylmethoxy)propyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

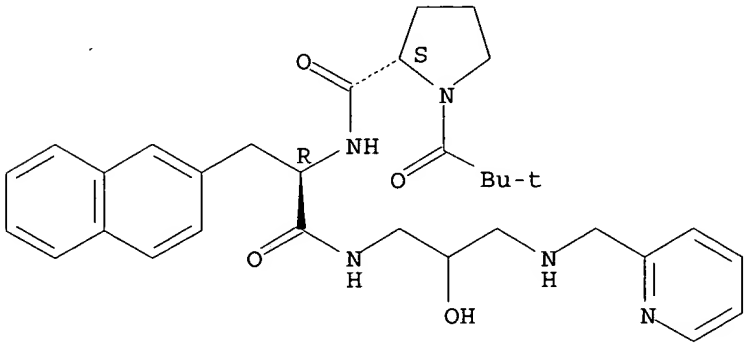
Absolute stereochemistry.



● HCl

RN 289048-99-3 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[2-hydroxy-3-[(2-pyridinylmethyl)amino]propyl]-3-(2-naphthalenyl)-, dihydrochloride (9CI) (CA INDEX NAME)

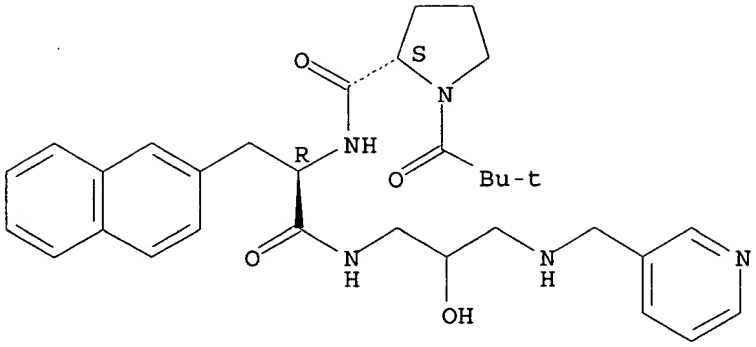
Absolute stereochemistry.



●2 HCl

RN 289049-00-9 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[2-hydroxy-3-[(3-pyridinylmethyl)amino]propyl]-3-(2-naphthalenyl)-, dihydrochloride (9CI) (CA INDEX NAME)

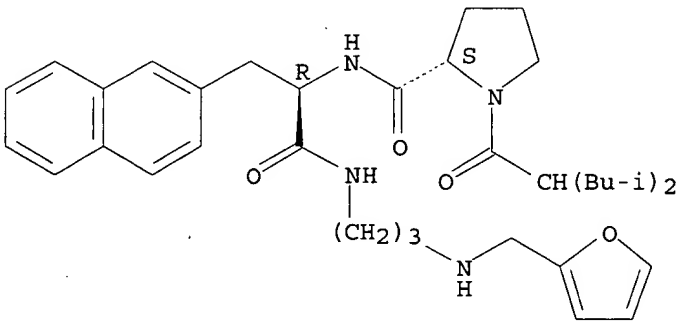
Absolute stereochemistry.



●2 HCl

RN 289049-01-0 HCAPLUS
CN D-Alaninamide, 1-[4-methyl-2-(2-methylpropyl)-1-oxopentyl]-L-prolyl-N-[3-[(2-furanylmethyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

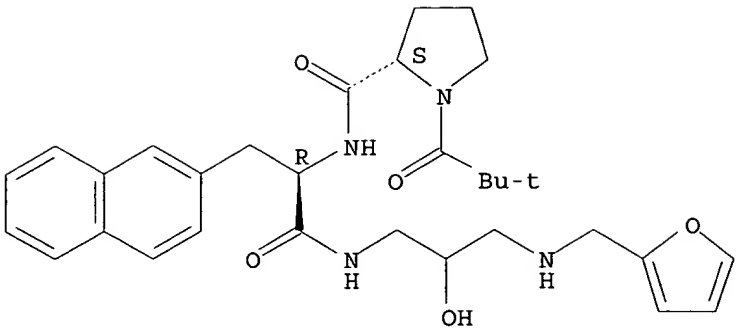
Absolute stereochemistry.



● HCl

RN 289049-02-1 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-[(2-furanylmethyl)amino]-2-hydroxypropyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

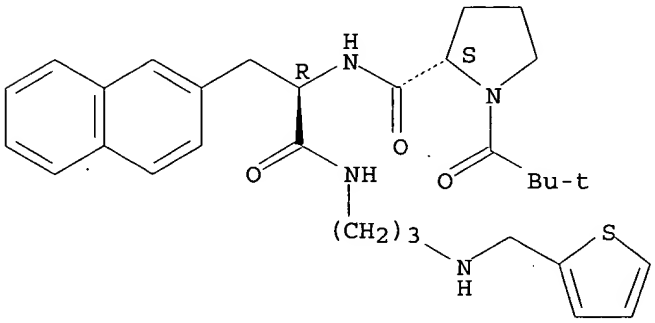
Absolute stereochemistry.



● HCl

RN 289049-03-2 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-3-(2-naphthalenyl)-N-[3-[(2-thienylmethyl)amino]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

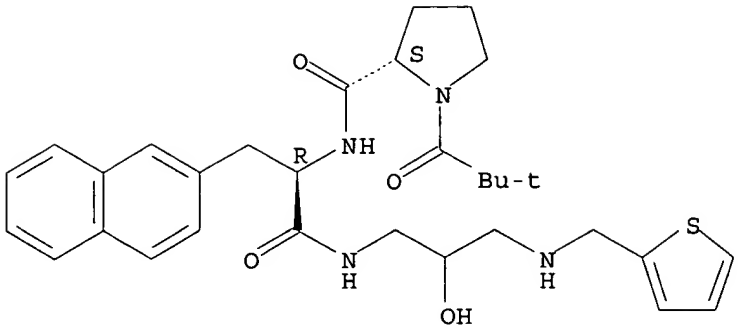
Absolute stereochemistry.



● HCl

RN 289049-04-3 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[2-hydroxy-3-[(2-thienylmethyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

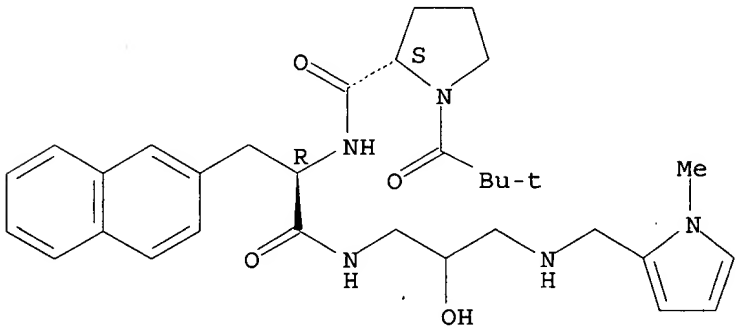
Absolute stereochemistry.



● HCl

RN 289049-05-4 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[2-hydroxy-3-[[(1-methyl-1H-pyrrol-2-yl)methyl]amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

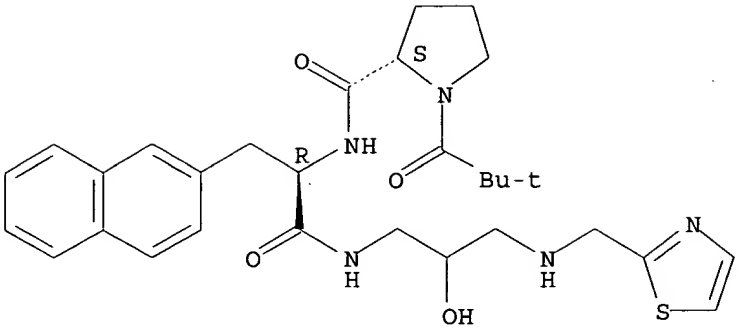
Absolute stereochemistry.



● HCl

RN 289049-06-5 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[2-hydroxy-3-[(2-thiazolylmethyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

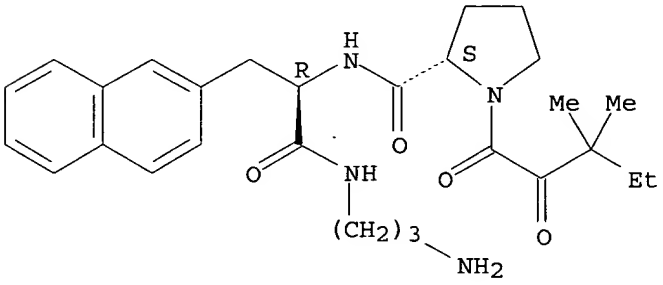
Absolute stereochemistry.



● HCl

RN 289049-08-7 HCAPLUS
CN D-Alaninamide, 1-(3,3-dimethyl-1,2-dioxopentyl)-L-prolyl-N-(3-aminopropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

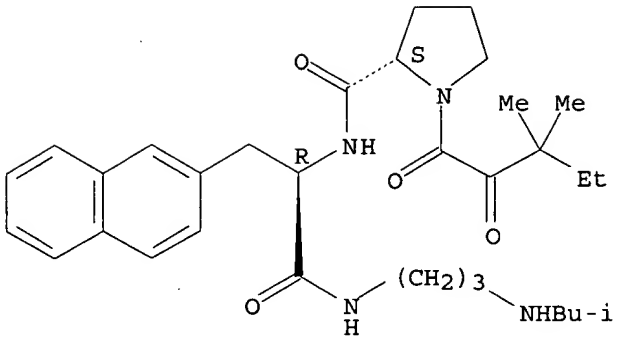
Absolute stereochemistry.



● HCl

RN 289049-09-8 HCAPLUS
CN D-Alaninamide, 1-(3,3-dimethyl-1,2-dioxopentyl)-L-prolyl-N-[3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

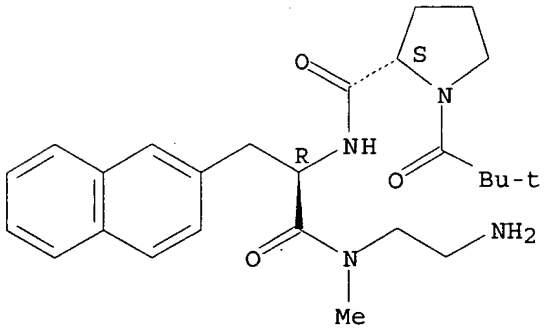
Absolute stereochemistry.



● HCl

RN 289049-20-3 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-(2-aminoethyl)-N-methyl-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

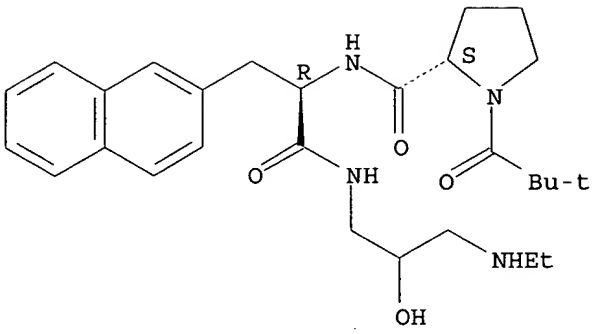
Absolute stereochemistry.



● HCl

RN 289049-21-4 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[3-(ethylamino)-2-hydroxypropyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

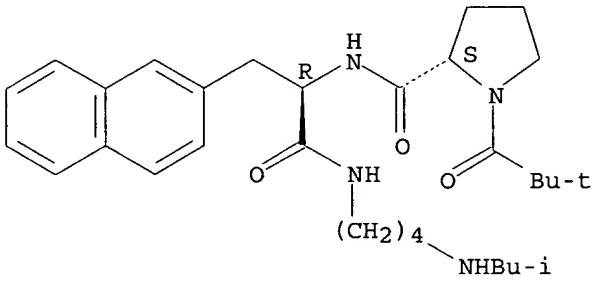
Absolute stereochemistry.



● HCl

RN 289049-22-5 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[4-[(2-methylpropyl)amino]butyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

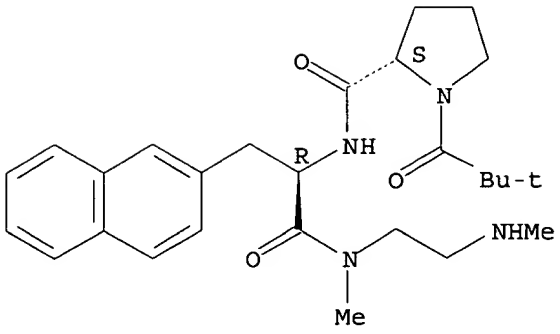
Absolute stereochemistry.



● HCl

RN 289049-23-6 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-methyl-N-[2-(methylamino)ethyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

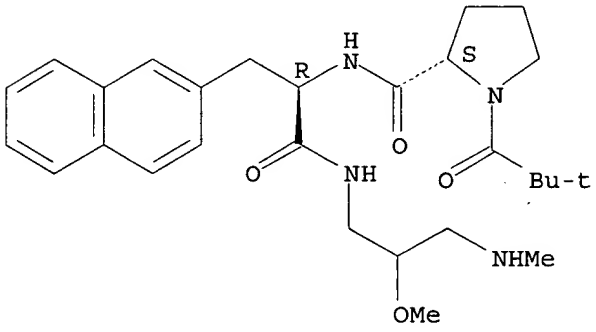
Absolute stereochemistry.



● HCl

RN 289049-24-7 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[2-methoxy-3-(methylamino)propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

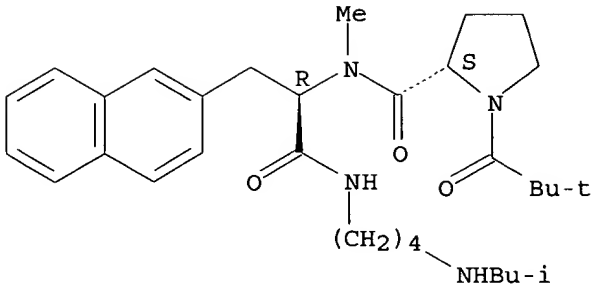
Absolute stereochemistry.



● HCl

RN 289049-25-8 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N2-methyl-N-[4-[(2-methylpropyl)amino]butyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

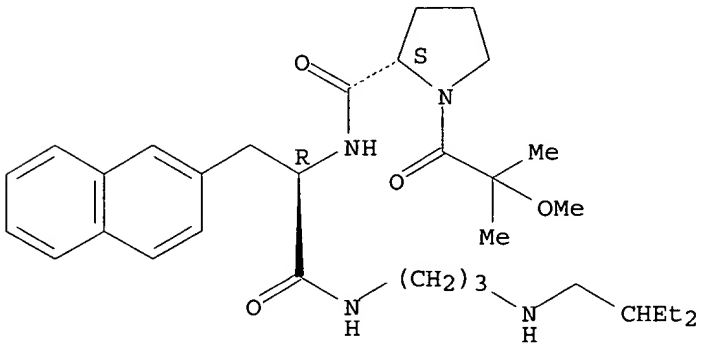
Absolute stereochemistry.



● HCl

RN 289049-26-9 HCAPLUS
CN D-Alaninamide, 1-(2-methoxy-2-methyl-1-oxopropyl)-L-prolyl-N-[3-[(2-ethylbutyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

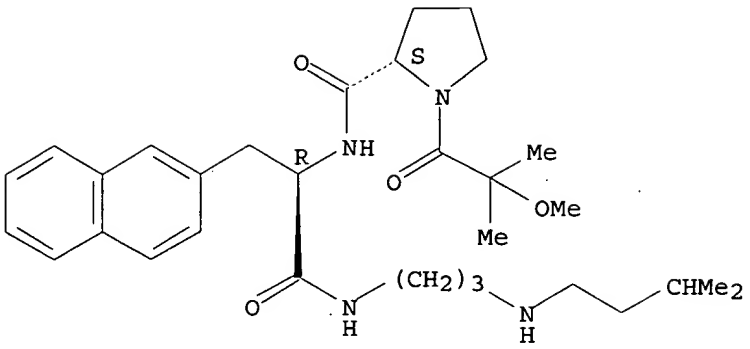
Absolute stereochemistry.



● HCl

RN 289049-27-0 HCAPLUS
CN D-Alaninamide, 1-(2-methoxy-2-methyl-1-oxopropyl)-L-prolyl-N-[3-[(3-methylbutyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

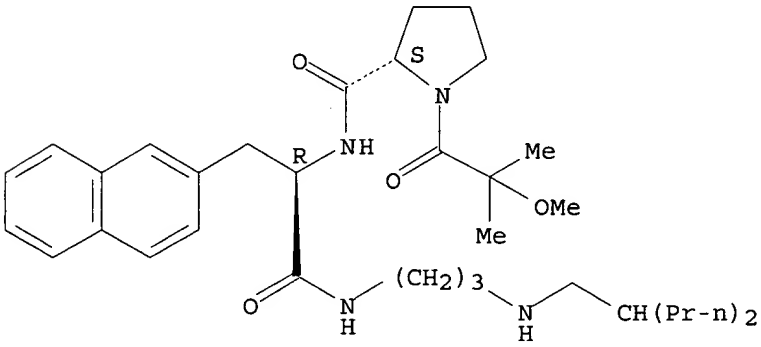
Absolute stereochemistry.



● HCl

RN 289049-28-1 HCAPLUS
CN D-Alaninamide, 1-(2-methoxy-2-methyl-1-oxopropyl)-L-prolyl-3-(2-naphthalenyl)-N-[3-[(2-propylpentyl)amino]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

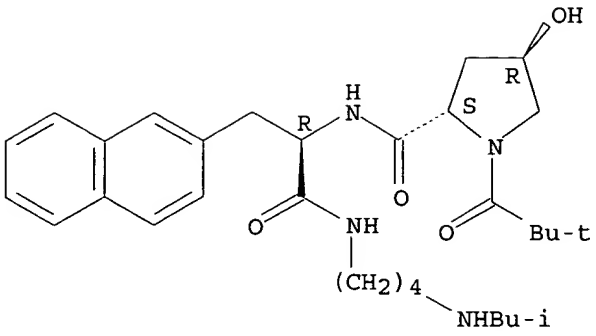
Absolute stereochemistry.



● HCl

RN 289049-29-2 HCAPLUS
CN D-Alaninamide, (4R)-1-(2,2-dimethyl-1-oxopropyl)-4-hydroxy-L-prolyl-N-[4-[(2-methylpropyl)amino]butyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

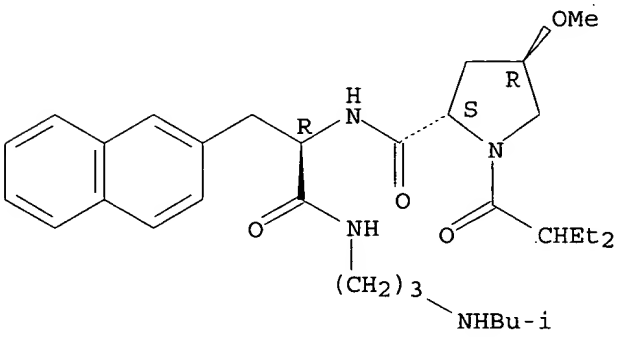
Absolute stereochemistry.



● HCl

RN 289049-30-5 HCAPLUS
CN D-Alaninamide, (4R)-1-(2-ethyl-1-oxobutyl)-4-methoxy-L-prolyl-N-[3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

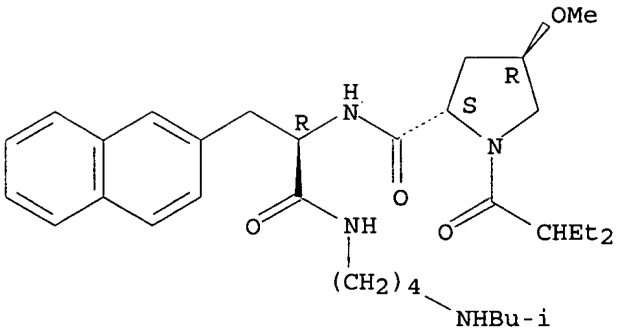
Absolute stereochemistry.



● HCl

RN 289049-31-6 HCAPLUS
CN D-Alaninamide, (4R)-1-(2-ethyl-1-oxobutyl)-4-methoxy-L-prolyl-N-[4-[(2-methylpropyl)amino]butyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

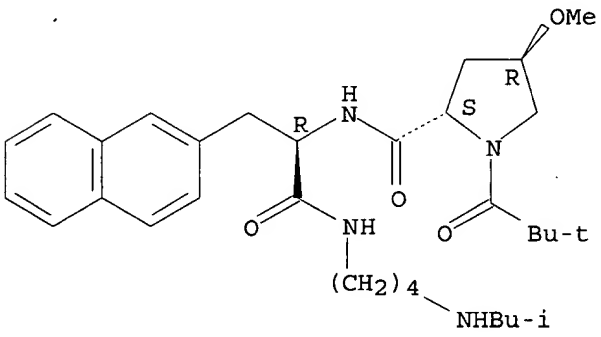
Absolute stereochemistry.



● HCl

RN 289049-32-7 HCAPLUS
CN D-Alaninamide, (4R)-1-(2,2-dimethyl-1-oxopropyl)-4-methoxy-L-prolyl-N-[4-[(2-methylpropyl)amino]butyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

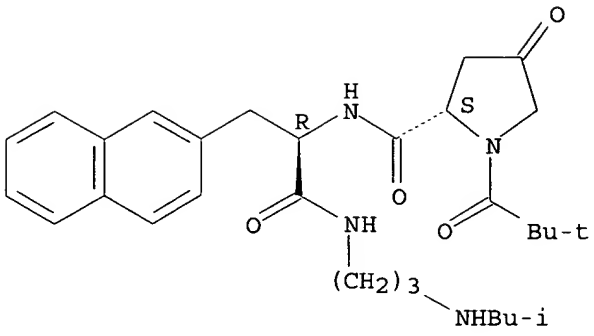
Absolute stereochemistry.



● HCl

RN 289049-33-8 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-4-oxo-L-prolyl-N-[3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

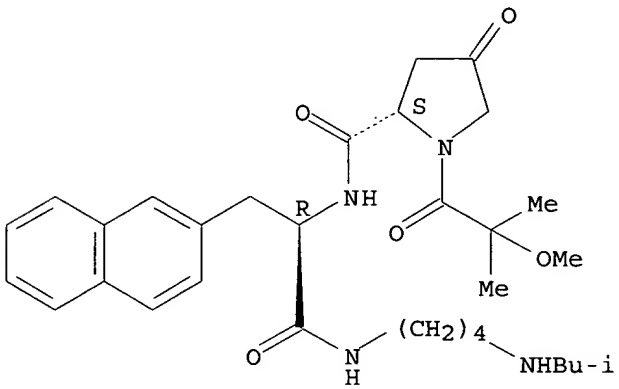
Absolute stereochemistry.



● HCl

RN 289049-34-9 HCAPLUS
CN D-Alaninamide, 1-(2-methoxy-2-methyl-1-oxopropyl)-4-oxo-L-prolyl-N-[4-[(2-methylpropyl)amino]butyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

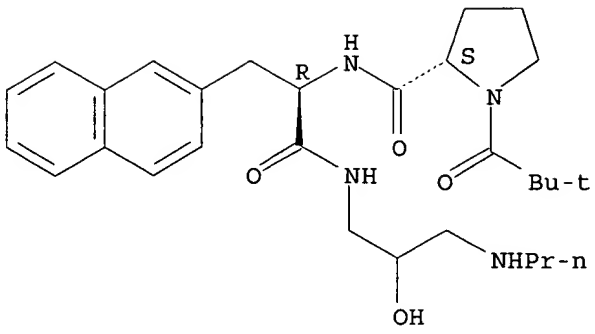
Absolute stereochemistry.



● HCl

RN 289049-36-1 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[2-hydroxy-3-(propylamino)propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

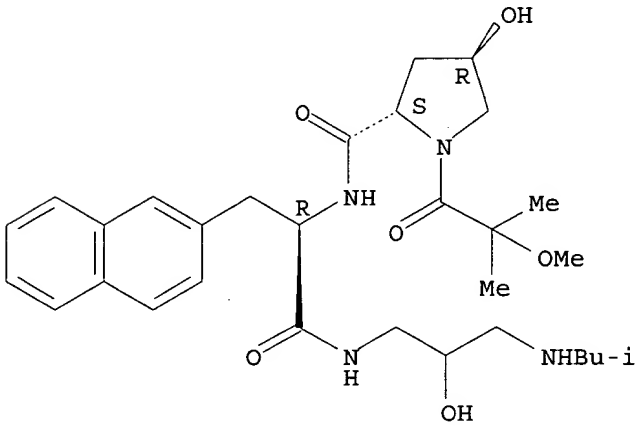
Absolute stereochemistry.



● HCl

RN 289049-37-2 HCAPLUS
CN D-Alaninamide, (4R)-4-hydroxy-1-(2-methoxy-2-methyl-1-oxopropyl)-L-prolyl-N-[2-hydroxy-3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

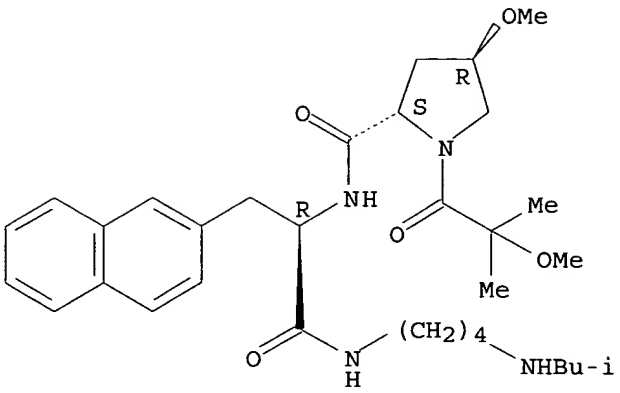
Absolute stereochemistry.



● HCl

RN 289049-38-3 HCAPLUS
CN D-Alaninamide, (4R)-4-methoxy-1-(2-methoxy-2-methyl-1-oxopropyl)-L-prolyl-N-[4-[(2-methylpropyl)amino]butyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

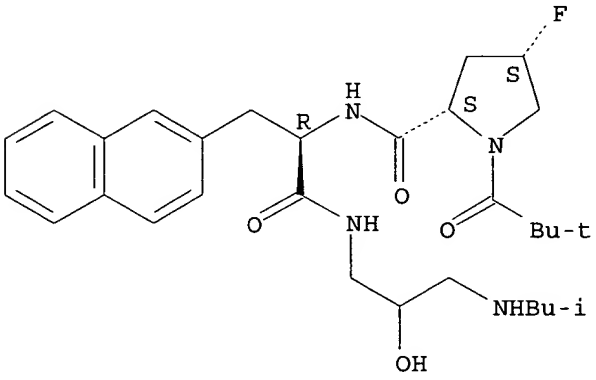
Absolute stereochemistry.



● HCl

RN 289049-40-7 HCAPLUS
CN D-Alaninamide, (4S)-1-(2,2-dimethyl-1-oxopropyl)-4-fluoro-L-prolyl-N-[2-hydroxy-3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

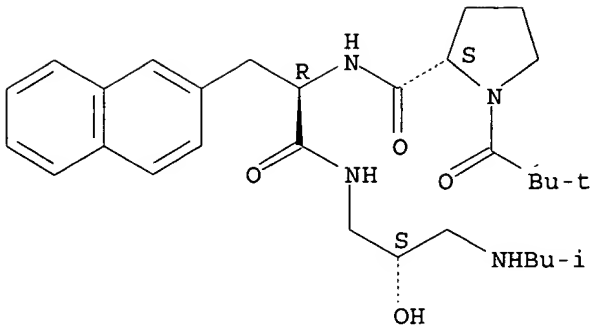
Absolute stereochemistry.



● HCl

RN 289049-41-8 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[(2S)-2-hydroxy-3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

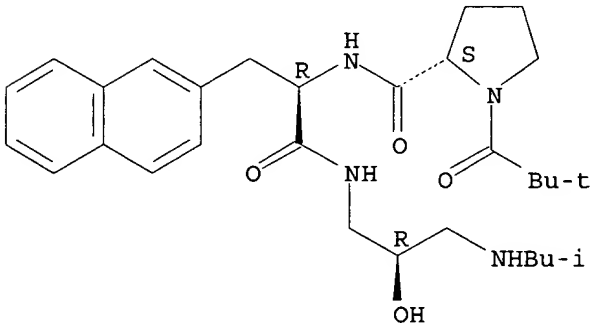
Absolute stereochemistry.



● HCl

RN 289049-42-9 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[(2R)-2-hydroxy-3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

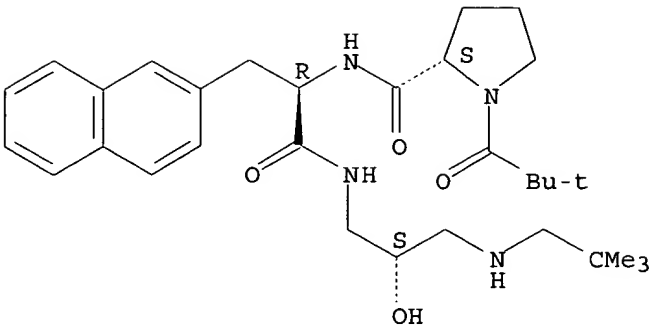
Absolute stereochemistry.



● HCl

RN 289049-43-0 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[(2S)-3-[(2,2-dimethylpropyl)amino]-2-hydroxypropyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

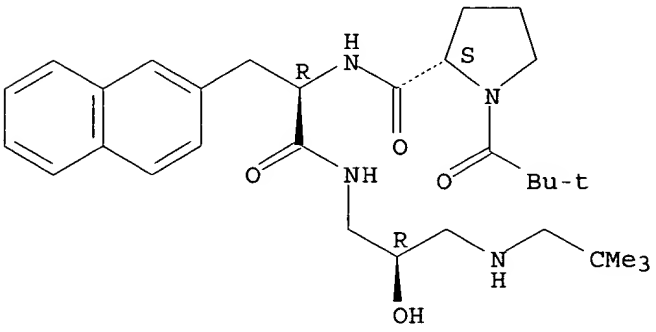
Absolute stereochemistry.



● HCl

RN 289049-44-1 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[(2R)-3-[(2,2-dimethylpropyl)amino]-2-hydroxypropyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

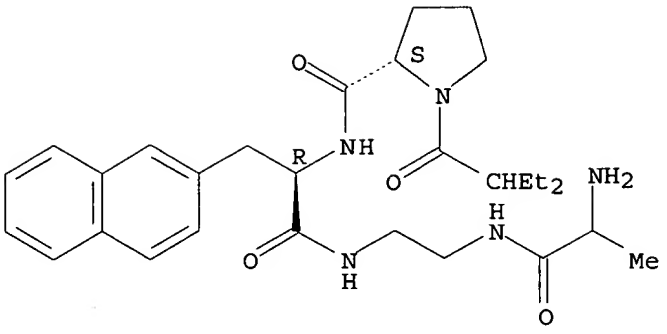
Absolute stereochemistry.



● HCl

RN 289049-46-3 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[2-[(2-amino-1-oxopropyl)amino]ethyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

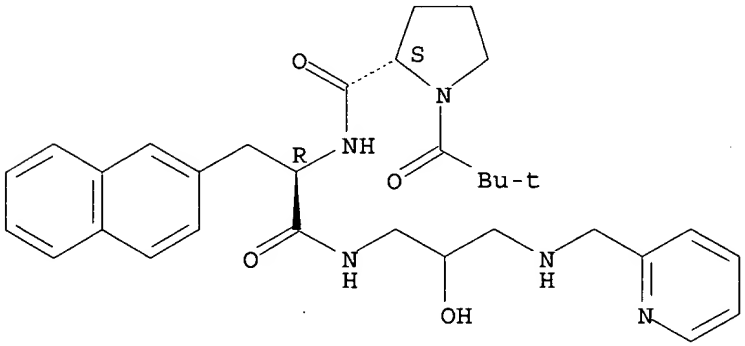
Absolute stereochemistry.



● HCl

RN 289050-17-5 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[2-hydroxy-3-[(2-pyridinylmethyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

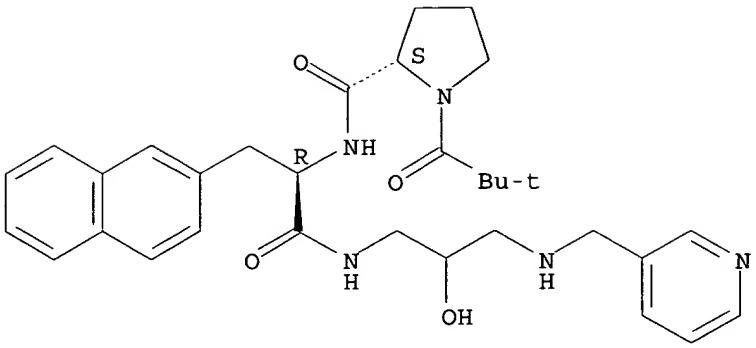
Absolute stereochemistry.



● HCl

RN 289050-24-4 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-[2-hydroxy-3-[(3-pyridinylmethyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

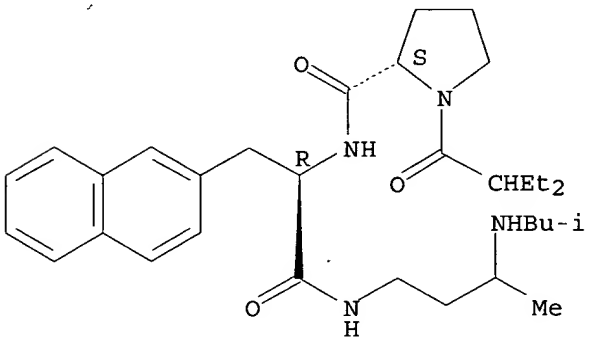
Absolute stereochemistry.



● HCl

RN 289050-31-3 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[3-[(2-methylpropyl)amino]butyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

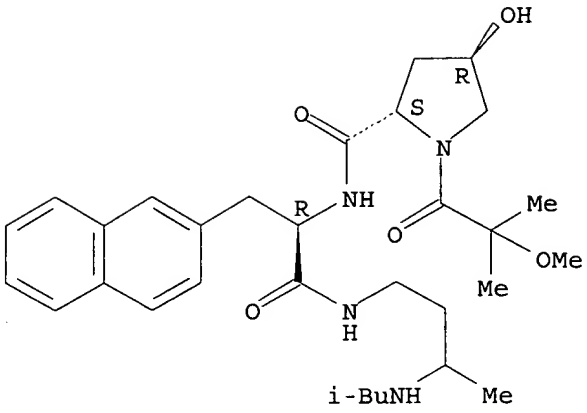
Absolute stereochemistry.



● HCl

RN 289050-46-0 HCAPLUS
CN D-Alaninamide, (4R)-4-hydroxy-1-(2-methoxy-2-methyl-1-oxopropyl)-L-prolyl-N-[3-[(2-methylpropyl)amino]butyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

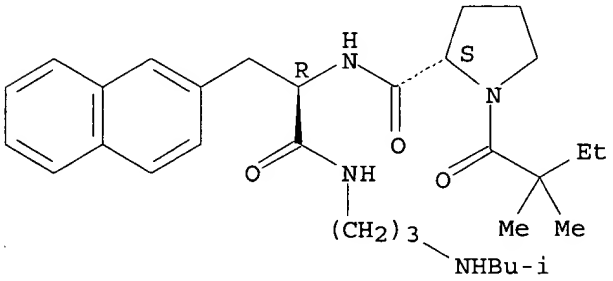
Absolute stereochemistry.



● HCl

RN 289050-56-2 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxobutyl)-L-prolyl-N-[3-[(2-methylpropyl)amino]propyl]-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

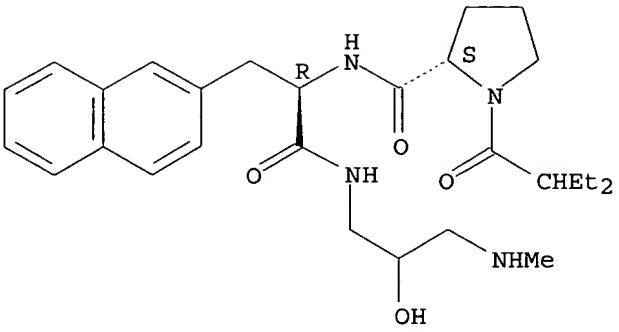
Absolute stereochemistry.



● HCl

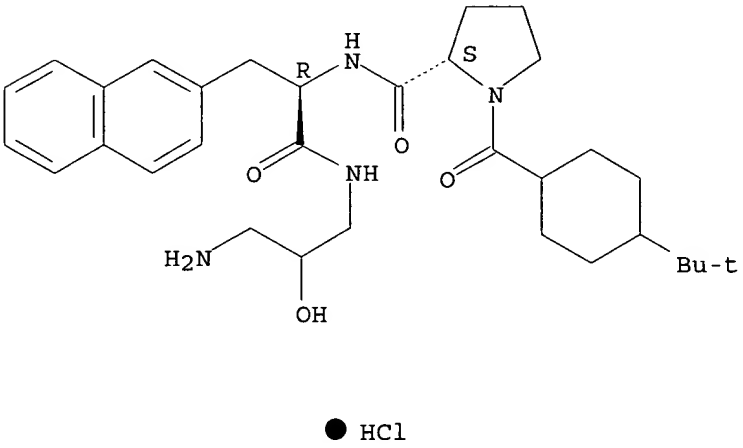
RN 289050-93-7 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[2-hydroxy-3-(methylamino)propyl]-3-(2-naphthalenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



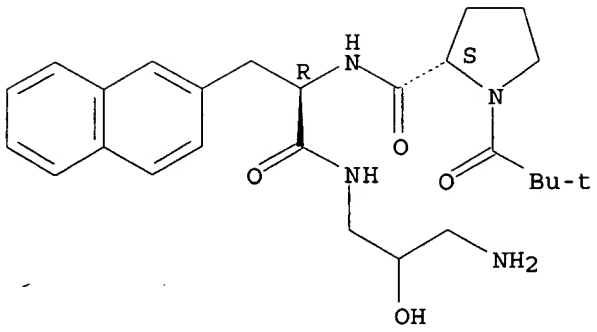
RN 289477-13-0 HCAPLUS
CN D-Alaninamide, 1-[[4-(1,1-dimethylethyl)cyclohexyl]carbonyl]-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



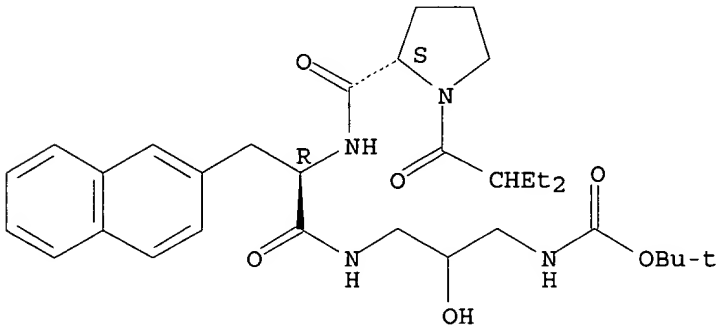
IT **289050-98-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of novel peptidomimetics as growth hormone secretagogues)
RN 289050-98-2 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



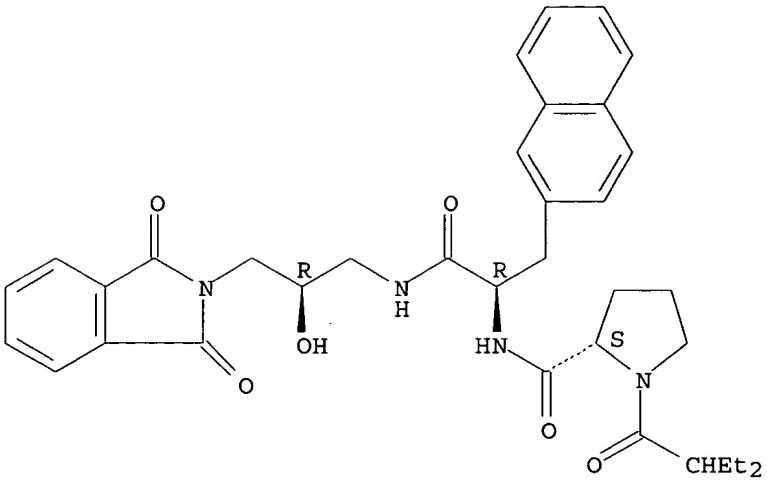
IT **289050-85-7P 289050-87-9P 289050-89-1P**
289050-91-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of novel peptidomimetics as growth hormone secretagogues)
RN 289050-85-7 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[3-[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxypropyl]-3-(2-naphthalenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



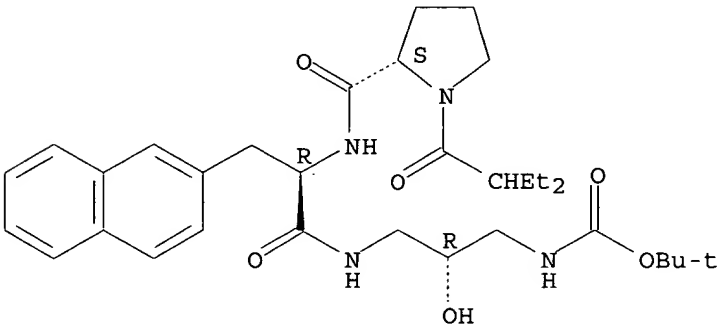
RN 289050-87-9 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[(2R)-3-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-2-hydroxypropyl]-3-(2-naphthalenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



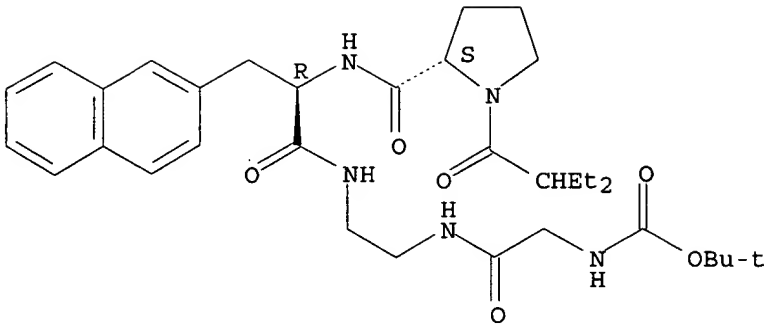
RN 289050-89-1 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[(2R)-3-[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxypropyl]-3-(2-naphthalenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 289050-91-5 HCAPLUS
CN D-Alaninamide, 1-(2-ethyl-1-oxobutyl)-L-prolyl-N-[2-[[[[(1,1-dimethylethoxy)carbonyl]amino]acetyl]amino]ethyl]-3-(2-naphthalenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L115 ANSWER 2 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:142982 HCAPLUS
DOCUMENT NUMBER: 140:187410
TITLE: Myocardial cell protecting agents
INVENTOR(S): Murata, Takahiko; Amakawa, Masahiro; Ikegami, Reiko; Ohyama, Tadashi; Ueo, Haruyoshi
PATENT ASSIGNEE(S): Kaken Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014412	A1	20040219	WO 2003-JP10158	20030808

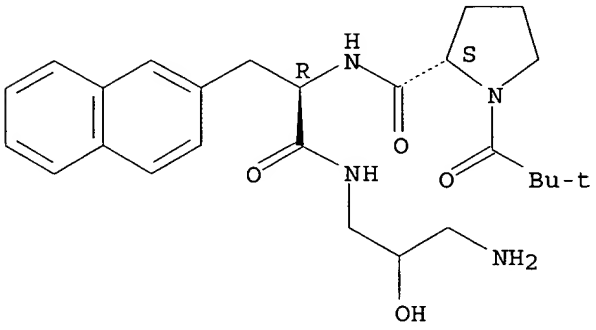
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2002-234029 A 20020809

AB It is intended to provide a preventive or a remedy for conditions associated with myocardial cell death characterized by containing, as the active ingredient, a ghrelin receptor agonist selected from the group consisting of ghrelin, ghrelin analogs, nonpeptidic compds. and pharmacol. acceptable salts thereof. This preparation directly acts on myocardial cells and inhibits cell death (necrosis and apoptosis) in a heart disease associated with myocardial cell death or the conditions of the heart associated with myocardial cell death caused by a heart surgery such as a heart bypass, thereby quickly inhibiting cell death of remaining myocardial cells even in a severe heart disease such as heart infarction, heart enlargement, myocarditis, etc. Thus, it exerts an excellent immediate action of preventing the progress of such a disease into heart failure. The effect of ghrelin, S-38855, MK-0677, NN-703, and CP 424391 on cultured H9c2 cell death was examined

ED Entered STN: 22 Feb 2004
IT **289050-98-2**, S 38855
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(myocardial cell protecting agents containing ghrelin, ghrelin analogs, and nonpeptidic compds.)
RN 289050-98-2 HCAPLUS
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L115 ANSWER 3 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:489260 HCAPLUS
DOCUMENT NUMBER: 135:87186
TITLE: Growth hormone liberation promoters as nerve protective drugs
INVENTOR(S): Murata, Takahiko; Ohyama, Tadashi; Amakawa, Masahiro; Fujita, Keiko; Ueo, Haruyoshi
PATENT ASSIGNEE(S): Kaken Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047558	A1	20010705	WO 2000-JP9431	20001228
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2395996	AA	20010705	CA 2000-2395996	20001228
AU 2001024054	A5	20010709	AU 2001-24054	20001228
EP 1258250	A1	20021120	EP 2000-987803	20001228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

US 2003100494	A1	20030529	US 2002-169423		20020627
PRIORITY APPLN. INFO.:			JP 1999-375513	A	19991228
			WO 2000-JP9431	W	20001228

AB Disclosed are preventives/remedies for diseases associated with the denaturation or death of nerve cells characterized by containing a growth hormone liberation promoter as the active ingredient. KP-102 (growth hormone-releasing peptide) reduced the size of cerebral infarct in ischemia-reperfusion rat model.

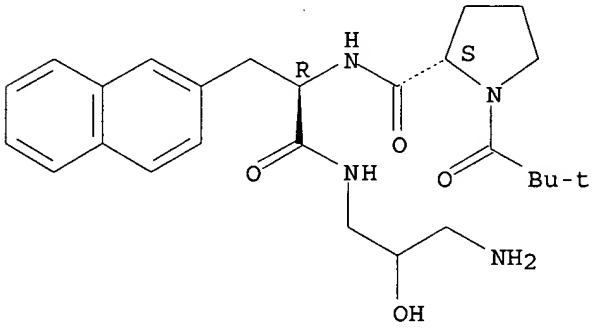
ED Entered STN: 06 Jul 2001

IT **289050-98-2**, S 38855 **348112-78-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(growth hormone liberation promoters as nerve protective drugs)

RN 289050-98-2 HCAPLUS

CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)- (9CI) (CA INDEX NAME)

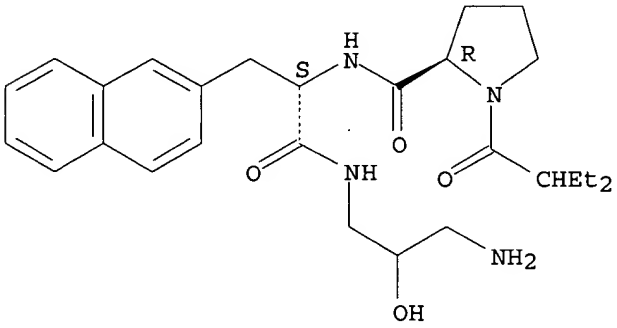
Absolute stereochemistry.



RN 348112-78-7 HCAPLUS

CN L-Alaninamide, 1-(2-ethyl-1-oxobutyl)-D-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Currently available stereo shown.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr 4
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, USPATFULL, MEDLINE, BIOSIS, EMBASE, WPIX' - CONTINUE? (Y)/N:y

L115 ANSWER 4 OF 28 USPATFULL on STN
ACCESSION NUMBER: 2003:146747 USPATFULL
TITLE: Nerve protective drugs
INVENTOR(S): Murata, Takahiko, Kyoto, JAPAN
Ohyama, Tadashi, Kyoto, JAPAN
Amakawa, Masahiro, Kyoto, JAPAN
Fujita, Keiko, Tokyo, JAPAN
Ueo, Haruyoshi, Kyoto, JAPAN

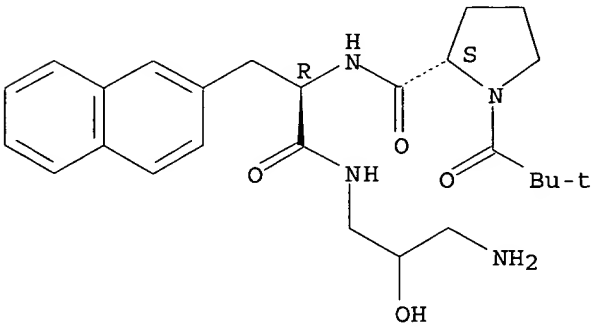
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003100494	A1	20030529	
APPLICATION INFO.:	US 2002-169423	A1	20020627	(10)
	WO 2000-JP9431		20001228	

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1999-375513	19991228

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: NIXON PEABODY LLP, ATTENTION: DAVID RESNICK, 101 FEDERAL STREET, BOSTON, MA, 02110
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 1073
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An agent for prevention or treatment of diseases involving degeneration or death of nerve cells, characterized by containing a growth hormone secretion promoting substance as an active ingredient, is provided.

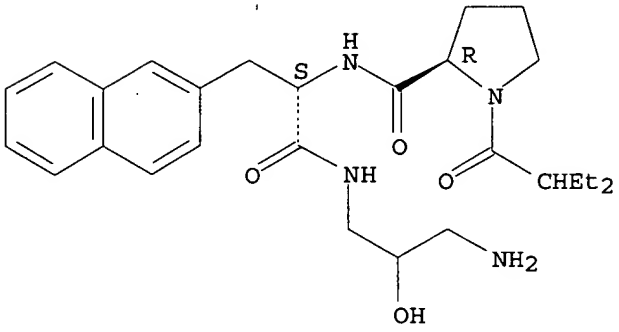
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **289050-98-2**, S 38855 **348112-78-7**
(growth hormone liberation promoters as nerve protective drugs)
RN 289050-98-2 USPATFULL
CN D-Alaninamide, 1-(2,2-dimethyl-1-oxopropyl)-L-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 348112-78-7 USPATFULL
CN L-Alaninamide, 1-(2-ethyl-1-oxobutyl)-D-prolyl-N-(3-amino-2-hydroxypropyl)-3-(2-naphthalenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Currently available stereo shown.



=> d ibib abs ed 5-14
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, USPATFULL, MEDLINE, BIOSIS, EMBASE, WPIX' - CONTINUE? (Y)/N:y

L115 ANSWER 5 OF 28 MEDLINE on STN
ACCESSION NUMBER: 2004570999 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15501059
TITLE: Synthesis and biological evaluation of an orally active ghrelin agonist that stimulates food consumption and adiposity in rats.
AUTHOR: Lugar Charles W; Clay Michael P; Lindstrom Terry D; Woodson Andrea L; Smiley David; Heiman Mark L; Dodge Jeffrey A
CORPORATE SOURCE: Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN 46285, USA.
SOURCE: Bioorganic & medicinal chemistry letters, (2004 Dec 6) 14 (23) 5873-6.
Journal code: 9107377. ISSN: 0960-894X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20041117
Last Updated on STN: 20041219

AB 2-(2-Amino-2-methyl-propionylamino)-5-phenyl-pentanoic acid [1-[1-(4-methoxy-phenyl)-1-methyl-2-oxo-2-pyrrolidin-1-yl-ethyl]-1H-imidazol-4-yl]-**amide** (LY444711, 6) is an orally active ghrelin agonist that binds with high affinity to and is a potent activator of the **growth hormone secretagogue** receptor 1a (GHS-R1a) receptor. In rat models of feeding behavior and pharmacology, 6 creates a positive energy balance and induces adiposity by stimulating food consumption and sparing fat utilization. As an orally active ghrelin agonist, 6 represents a new pharmacological tool to investigate the orexigenic role of ghrelin in regulating energy homeostasis.

ED Entered STN: 20041117
Last Updated on STN: 20041219

L115 ANSWER 6 OF 28 MEDLINE on STN
ACCESSION NUMBER: 2003303829 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12831762
TITLE: Identification of tilapia ghrelin and its effects on growth hormone and prolactin release in the tilapia, Oreochromis mossambicus.
AUTHOR: Kaiya Hiroyuki; Kojima Masayasu; Hosoda Hiroshi; Riley Larry G; Hirano Tetsuya; Grau E Gordon; Kangawa Kenji
CORPORATE SOURCE: Department of Biochemistry, National Cardiovascular Center Research Institute, 5-7-1 Fujishirodai, Osaka 565-8565, Suita, Japan.. kaiya@ri.ncvc.go.jp
SOURCE: Comparative biochemistry and physiology. Part B, Biochemistry & molecular biology, (2003 Jul) 135 (3) 421-9. Journal code: 9516061. ISSN: 1096-4959.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 20030701
Last Updated on STN: 20040318
Entered Medline: 20040317
AB We have identified ghrelin and cDNA encoding precursor protein from the stomach of a euryhaline tilapia, Oreochromis mossambicus. The sequence of 20-amino acid tilapia ghrelin is GSSFLSPSQKPQNKVKSSRI. The third serine residue was modified by n-decanoic acid. The carboxyl-terminal end of the peptide possessed an **amide** structure. RT-PCR analysis revealed high levels of gene expression in the stomach and low levels in the brain, kidney and gill. Tilapia ghrelin stimulated growth hormone (GH) and prolactin (PRL) release from the organ-cultured tilapia pituitary at a dose of 10 nM. Thus, a novel regulatory mechanism of GH secretion by gastric ghrelin seems to be conserved in the tilapia. Stimulation of PRL release by homologous ghrelin has been reported in human, bullfrog and eel, and suggests the presence of **growth hormone secretagogue** receptor not only on somatotrophs but also on PRL cells of the tilapia pituitary.
ED Entered STN: 20030701
Last Updated on STN: 20040318
Entered Medline: 20040317

L115 ANSWER 7 OF 28 MEDLINE on STN
ACCESSION NUMBER: 2002216136 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11951975
TITLE: Tandem mass spectrum of a **growth hormone secretagogue**: **amide** bond cleavage and resultant gas-phase rearrangement.
AUTHOR: Qin Xue-Zhi
CORPORATE SOURCE: Pharmaceutical Research, Merck Research Laboratories, West Point, Pennsylvania 19486, USA.. zuezhi_qin@merck.com
SOURCE: Journal of the American Society for Mass Spectrometry, (2002 Apr) 13 (4) 371-7. Journal code: 9010412. ISSN: 1044-0305.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020416
Last Updated on STN: 20020501

Entered Medline: 20020430

AB Compound 1 [N-[1(R)-[(1,2-dihydro-1-methylsulfonylspiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-2-(phenylmethyloxy)ethyl]-2-amino-2-methylpropanamide](MW 528) is an orally-active **growth hormone secretagogue** (GHS). As part of a continual effort to analyze the ESI/MS and MSn data of novel drugs, the ESI/MS and MS/MS data of protonated 1 (m/z 529) are analyzed and reported here. The analyses reveal that under low-energy collision-induced dissociation (CID) in an ion trap or a quadrupole collision cell, protonated 1 undergoes a gas-phase rearrangement to form protonated 3 (m/z 357) which competes with the y- and b-type product ions during the **amide** bond cleavages of protonated 1. It is proposed that when the b-type ion is formed by cleavage of the piperidine **amide** bond, piperidine (a neutral species) and the b-ion (a cation) form an ion-neutral complex. In this complex, piperidine functions as a nucleophile to attack the benzylic carbon of the b-ion, and the protonated ether group in the b-ion acts as a leaving group, which results in the migration of the benzylic group to the piperidine amine to form protonated 3. Protonated 2 (an analog of 1) was studied under the same experimental conditions. The results show that protonated 2 undergoes a similar rearrangement to form protonated 3. While this rearrangement is a relatively minor fragmentation process for protonated 1, it is a predominant process for protonated 2. This phenomenon is explained in terms of the proposed ion-neutral-complex mechanism.

ED Entered STN: 20020416
Last Updated on STN: 20020501
Entered Medline: 20020430

L115 ANSWER 8 OF 28 MEDLINE on STN
ACCESSION NUMBER: 2001230085 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11322496
TITLE: Recombinant human GHRH(1-44)NH2: clinical utility and therapeutic development program.
AUTHOR: Ehlers M R
CORPORATE SOURCE: BioNebraska, Inc., Lincoln, NE 68524, USA.. mehlers@bionebraska.com
SOURCE: Endocrine, (2001 Feb) 14 (1) 137-41.
Journal code: 9434444. ISSN: 0969-711X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010827
Last Updated on STN: 20010827
Entered Medline: 20010823

AB **Growth hormone** (GH) **secretagogues** are becoming increasingly attractive alternatives to GH or insulin-like growth factor-I (IGF-I) for the treatment of conditions that may benefit from activation of the GH/IGF-I axis. This stems from the realization that (1) GH secretagogues stimulate the pulsatile release of endogenous GH; (2) feedback control of endogenous GH and IGF-I is preserved, guarding against imbalances between GH and IGF-I levels; and (3) GH treatment is associated with adverse effects in the elderly. Of the GH **secretagogues**, **growth hormone**-releasing **hormone** (GHRH) remains the best characterized, in terms of identity of the ligand-receptor pair and its exclusive somatotropic activity at the level of the pituitary. Full-length natural GHRH (1-44) **amide** can now be produced by recombinant technologly on a commercially viable scale, and is currently being evaluated in early phase clinical trials. The purpose

of these studies is to evaluate the efficacy and tolerability of chronic subcutaneous administration of GHRH over a range of doses in elderly subjects. Therapeutic areas that are being investigated in the elderly include congestive heart failure, osteoporosis, and improvements in body composition and function in the frail elderly.
ED Entered STN: 20010827
Last Updated on STN: 20010827
Entered Medline: 20010823

L115 ANSWER 9 OF 28 MEDLINE on STN
ACCESSION NUMBER: 1999270442 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10340617
TITLE: New growth hormone secretagogues: C-terminal modified sulfonamide-analogues of NN703.
AUTHOR: Peschke B; Hansen B S
CORPORATE SOURCE: Health Care Chemistry, Novo Nordisk A/S, Novo Nordisk Park, Malov, Denmark.. bpes@novo.dk
SOURCE: Bioorganic & medicinal chemistry letters, (1999 May 3) 9 (9) 1295-8.
Journal code: 9107377. ISSN: 0960-894X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990827
Last Updated on STN: 19990827
Entered Medline: 19990819
AB The C-terminal the orally active **growth hormone secretagogue** NN703 was changed to prepare analogues with inverse sulfonamides and inverse **amides.** The compounds showed high activity in a in vitro rat pituitary model.
ED Entered STN: 19990827
Last Updated on STN: 19990827
Entered Medline: 19990819

L115 ANSWER 10 OF 28 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 1997:70217 BIOSIS
DOCUMENT NUMBER: PREV199799369420
TITLE: Benzolactam **growth hormone secretagogues**: Replacement of the C-3 **amide** bond in L-692,429.
AUTHOR(S): Ok, Hyun O. [Reprint author]; Szumiloski, John L.; Doldouras, George A.; Schoen, William R.; Cheng, Kang; Chan, Wanda W.-S.; Butler, Bridget S.; Smith, Roy G.; Fisher, Michael H.; Wyvratt, Matthew J.
CORPORATE SOURCE: Dep. Med. Chem., Merck Res. Lab., P.O. Box 2000, Rahway, NJ 07065, USA
SOURCE: Bioorganic and Medicinal Chemistry Letters, (1996) Vol. 6, No. 24, pp. 3051-3056.
CODEN: BMCLE8. ISSN: 0960-894X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Feb 1997
Last Updated on STN: 11 Feb 1997
AB The synthesis and structure-activity relationships of various C-3 **amide** bond modifications in the novel nonpeptidyl **growth hormone secretagogue** L-692,429 are described. Several C-3 **amide** surrogates were prepared and the urea moiety was found

to exhibit growth hormone releasing activity similar to that observed with L-692,429.
ED Entered STN: 11 Feb 1997
Last Updated on STN: 11 Feb 1997

L115 ANSWER 11 OF 28 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 1995:422524 BIOSIS
DOCUMENT NUMBER: PREV199598436824
TITLE: 3-Substituted benzolactam **growth hormone secretagogues**: Replacement of the C-3 **amide** bond moiety of L-692,429.
AUTHOR(S): Ok, Hyun O. [Reprint author]; Shih, Thomas L.; Szumiloski, John L.; Schoen, William R.; Cheng, Kang; Chan, Wanda W.-S.; Butler, Bridget S.; Smith, Roy G.; Fisher, Michael H.; Wyvratt, Matthew J.
CORPORATE SOURCE: Dep. Med. Chem. Biochem. Physiol., Merck Res. Lab., PO Box 2000, Rahway, NJ 07065, USA
SOURCE: Abstracts of Papers American Chemical Society, (1995) Vol. 210, No. 1-2, pp. MEDI 74.
Meeting Info.: 210th American Chemical Society National Meeting. Chicago, Illinois, USA. August 20-24, 1995.
CODEN: ACSRAL. ISSN: 0065-7727.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Oct 1995
Last Updated on STN: 1 Nov 1995
ED Entered STN: 3 Oct 1995
Last Updated on STN: 1 Nov 1995

L115 ANSWER 12 OF 28 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 1994:464204 BIOSIS
DOCUMENT NUMBER: PREV199497477204
TITLE: Michael additions of (R)-1-amino-2-propanol into very sterically hindered 3,3-dimethylacryl **amides**: Synthesis of **growth hormone secretagogue** L-692,585.
AUTHOR(S): Wells, K. M.; Rossen, K.; Hartner., F. W., Jr.; Askin, D.; Schoen, W. R.; Pisano, J. M.; Volante, R. P.; Reider, P. J.
CORPORATE SOURCE: Merck Res. Lab., P.O. Box 2000, Rahway, NJ 07065-0900, USA
SOURCE: Abstracts of Papers American Chemical Society, (1994) Vol. 208, No. 1-2, pp. ORGN 19.
Meeting Info.: 208th National Meeting of the American Chemical Society. Washington, D.C., USA. August 21-25, 1994.
CODEN: ACSRAL. ISSN: 0065-7727.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Oct 1994
Last Updated on STN: 16 Dec 1994
ED Entered STN: 31 Oct 1994
Last Updated on STN: 16 Dec 1994

L115 ANSWER 13 OF 28 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2002:502406 BIOSIS
DOCUMENT NUMBER: PREV200200502406

TITLE: New growth hormone secretagogues.
AUTHOR(S): Guerlavais, V.; Boeglin, D.; Fehrentz, J. A. [Reprint author]; Deghenghi, R.; Locatelli, V.; Martinez, J.
CORPORATE SOURCE: Laboratoire des Aminoacides, Peptides et Proteines (LAPP), Faculte de Pharmacie, UMR 5810, Universite Montpellier I et II, 15 Avenue Charles Flahaut, 34093, B.P. 14491, Montpellier Cedex 5, France
fehrentz@colombes.pharma.univ-montp1.fr
SOURCE: Letters in Peptide Science, (2001 (2002)) Vol. 8, No. 3-5, pp. 187-193. print.
ISSN: 0929-5666.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Sep 2002
Last Updated on STN: 25 Sep 2002
AB Starting from EP 51389, a potent **growth hormone secretagogue** (GHS), a new series of GHS has been designed, synthesized and tested. This series was built on a gem-diamino moiety and a structure activity relationship study was performed including N-methylation of the **amide** bonds. Some analogues exhibited more powerful activity than Hexarelin, they were active per os on dog and have been selected as candidates for further development.
ED Entered STN: 25 Sep 2002
Last Updated on STN: 25 Sep 2002

L115 ANSWER 14 OF 28 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2002277441 EMBASE
TITLE: New growth hormone secretagogues.
AUTHOR: Guerlavais V.; Boeglin D.; Fehrentz J.A.; Deghenghi R.; Locatelli V.; Martinez J.
CORPORATE SOURCE: J.A. Fehrentz, LAPP, UMR 5810, Universite Montpellier I et II, 15 avenue Charles Flahaut, 34093 Montpellier Cedex 5, France. fehrentz@colombes.pharma.univ-montpl.fr
SOURCE: Letters in Peptide Science, (2002) 8/3-5 (187-193).
Refs: 10
ISSN: 0929-5666 CODEN: LPSCEM
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 003 Endocrinology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Starting from EP 51389, a potent **growth hormone secretagogue** (GHS), a new series of GHS has been designed, synthesized and tested. This series was built on a gem-diamino moiety and a structure activity relationship study was performed including N-methylation of the **amide** bonds. Some analogues exhibited more powerful activity than Hexarelin, they were active per os on dog and have been selected as candidates for further development.

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YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, USPATFULL, MEDLINE, BIOSIS, EMBASE, WPIX' - CONTINUE? (Y)/N:y

YOU HAVE REQUESTED DATA FROM 14 ANSWERS - CONTINUE? Y/(N):y

L115 ANSWER 15 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-440877 [41] WPIX
DOC. NO. CPI: C2004-165246
TITLE: New prolyl urea and thiourea related compounds are androgen receptor modulators, useful for treating e.g. cachexia, eating disorders, depression, Syndrome X, diabetic complications and obesity.
DERWENT CLASS: B02 B03
INVENTOR(S): AUGERI, D J; HAMANN, L G; MANFREDI, M C
PATENT ASSIGNEE(S): (BRIM) BRISTOL-MYERS SQUIBB CO
COUNTRY COUNT: 107
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004045518	A2	20040603	(200441)*	EN	57	A61K000-00
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW						
AU 2003302084	A1	20040615	(200470)			A61K000-00

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004045518	A2	WO 2003-US36331	20031113
AU 2003302084	A1	AU 2003-302084	20031113

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2003302084	A1	Based on	WO 2004045518

PRIORITY APPLN. INFO: US 2002-426694P 20021115
INT. PATENT CLASSIF.:
MAIN: A61K000-00
BASIC ABSTRACT:
WO2004045518 A UPAB: 20040629
NOVELTY - Prolyl urea and thiourea related compounds (I) and their prodrugs, esters, salts and stereoisomers are new.
DETAILED DESCRIPTION - Prolyl urea and thiourea related compounds (I) and their prodrugs, esters, salts and stereoisomers are new.
R1 = H or CH2OR4; alkyl, alkenyl, cycloalkyl or arylalkyl (all optionally substituted);
R2 = H or CH2OR4; alkyl, alkenyl, arylalkyl, heterocyclo or (hetero)aryl (all optionally substituted);
R3 = H, optionally substituted alkyl, CH2OR4, OR2, SR2, halo, NHR2, NHCOR4, NHCO2R4, NHCONR4R4' or NHSO2R4;
R4, R4' = H; alkyl, alkenyl, alkynyl, cycloalkyl, arylalkyl, heterocyclo or (hetero)aryl (all optionally substituted);
G = a mono- or polycyclic ring system of heterocyclo or (hetero)aryl (where ring system is optionally substituted with H, halo, CN, CF3, OR4, CO2R4, NR4R4', CONR4R4', CH2OR4, SR4, SOR4, SO2R4 or NO2; alkyl, alkenyl, alkynyl, cycloalkyl, arylalkyl or (hetero)aryl (all optionally substituted));

X = a linking group selected from NR4 or CHR4;
Y = O, NR4, NOR4, S or CH;
Z = O or NR4;
n = 1-2;
provided that:
(1) when Y is NOR4, R4 is not H;
(2) compounds where R1 is CH3, X is NH, Y is O or S and Z is O are excluded;
(3) compounds where R1 is CH3, X is NH, Z is O, Y is NR4'' are excluded.
R4'' = alkyl, alkenyl, cycloalkyl, arylalkyl, heteroaryl (all optionally substituted); and
G = a group of formula (1).
R13 = H, CN, NO2, halo, heterocyclo, OR14, CO2R15, CONHR15, COR15, S(O)pR15, SO2NR15R15', NHCOR15 or NHSO2R15;
R14 = H, optionally substituted alkyl, CHF2, CF3 or COR15;
R15, R15' = alkyl, alkenyl, alkynyl, (hetero)cycloalkyl, arylalkyl or (hetero)aryl (all optionally substituted); H or CN;
A, B = H, halo, CN, NO2, optionally substituted alkyl or OR14; and
p = 0-2;
An INDEPENDENT CLAIM is also included for a pharmaceutical composition comprising (I) optionally in combination with a growth-promoting agent or at least one additional therapeutic agent.
ACTIVITY - Muscular-Gen.; Antilipemic; Osteopathic; Immunomodulator; Eating-Disorders-Gen.; Antidepressant; Tranquilizer; Nootropic; Endocrine-Gen.; Antianginal; Antidiabetic; Anorectic.
MECHANISM OF ACTION - Androgen receptor modulator.
USE - (I) are used to treat or delay the progression or onset of muscular atrophy, lipodystrophy, long-term critical illness, sarcopenia, frailty or age-related functional decline, reduced muscle strength and function, reduced bone density or growth, the catabolic side effects of glucocorticoids, chronic fatigue syndrome, bone fracture repair, acute fatigue syndrome and muscle loss following elective surgery, cachexia, chronic catabolic state, eating disorders, side effects of chemotherapy, wasting, depression, nervousness, irritability, stress, growth retardation, reduced cognitive function, male contraception, hypogonadism, Syndrome X, diabetic complications or obesity (claimed).
Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B01-C04; B01-C05; B06-H; **B07-D03**; B07-D05; B14-E11; B14-E12; B14-F06; B14-J01; B14-J05; B14-L01; B14-L06; B14-N01; B14-P01A; B14-S04

TECH UPTX: 20040629

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: Preparation of (I) comprises reaction of dihydropyrrole derivative of formula (II) with suitable coupling reagents, such as EDAC and 1-hydroxybenzotriazole hydrate together with HZR1 to form a compound of formula (III), followed by reaction of (III) with a compound of formula G-NCY to form (I; X = NH) (I'). (I') may be alkylated by treatment with a base such as NaH, followed by treatment with an electrophile such as R4-Br to give the alkylated compound of formula (I; X = NR4) (I'').

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The additional therapeutic agent is parathyroid hormone, bisphosphonates, estrogen, testosterone, progesterone, selective estrogen receptor modulators, **growth hormone secretagogues**, **growth hormone**, progesterone receptor modulators, anti-diabetic agents, anti-hypertensive agents, anti-inflammatory agents, anti-osteoporosis agents, anti-obesity agents, cardiac glycosides, cholesterol lowering

agents, anti-depressants, anti-anxiety agents, anabolic agents or thyroid mimetics.

ABEX UPTX: 20040629

SPECIFIC COMPOUNDS - 4 Compounds (I) are disclosed, e.g. 1-(4-cyanonaphthalen-1-ylcarbamoyl)-3-hydroxy-pyrrolidine-2-carboxylic acid methyl ester (Ia).

ADMINISTRATION - Dosage of (I) is 0.01-2000 mg/day, administered 1-4 times per day, orally, sublingually, bucally, parenterally, nasally, topically or rectally.

EXAMPLE - To 4-cyanonaphthylamine in dichloromethane (20 ml) was added sodium carbonate (1.94 g) followed by phosgene (9.80 ml) (20% solution in toluene) and the suspension was stirred at room temperature for 1 hour. Another 2.5 ml of 20% phosgene in toluene solution was added, and the suspension stirred for 1.5 hour. The reaction mixture was worked up to give 4-isocyanato-naphthalene-1-carbonitrile (a) (83 mg). To a suspension of (a) (0.51 g) in dichloromethane (2 ml) cooled to 0degreesC was added diisopropylethylamine (0.37 ml). After stirring at 0degreesC for 20 minutes, cis-3-hydroxyproline methyl ester (0.34 g) in dichloromethane (1 ml) solution was added, along with 4 Angstrom molecular sieves (0.5 g) and the resulting mixture was stirred at room temperature until urea formation was complete. The reaction mixture was worked up to give 1-(4-cyanonaphthalen-1-ylcarbamoyl)-3-hydroxypyrrolidine-2-carboxylic acid methyl ester (Ia) (436 mg), as a white foam.

DEFINITIONS - Preferred Definitions:
R8 = CN;
R1, R2 = H or alkyl;
G = heterocyclic compounds of formula (2-5);
R8-R11 = alkyl, alkenyl, alkynyl, cycloalkyl, arylalkyl, (hetero)aryl (all optionally substituted), H, NO2, CN, CF3, OR4, CO2R4, NR4R4', CONR4R4' or CH2OR4;
A-F = N or CR1;
J, K, L, P, Q = NR12, O, S, SO, SO2 or CR12R12';
R12 , R12' = bond or R1;
m = 0 or 1;
R3 = OH;
X = NR4;
Y, Z = O; and
n = 1.

L115 ANSWER 16 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-214287 [20] WPIX
DOC. NO. CPI: C2004-084783
TITLE: Composition used for treating and preventing diabetes, obesity and obesity-related disorders comprises neuropeptide Y antagonist and antiobesity agent.
DERWENT CLASS: B02 C02
INVENTOR(S): ISHIHARA, A; MACNEIL, D J; MCINTYRE, J H; VAN DER PLOEG, L H T
PATENT ASSIGNEE(S): (BANY) BANYU PHARM CO LTD; (MERI) MERCK & CO INC
COUNTRY COUNT: 104
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004009015	A2	20040129	(200420)*	EN	134	A61K000-00

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ
LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL
PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN
YU ZA ZM ZW

AU 2003253925 A1 20040209 (200450) A61K000-00

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004009015	A2	WO 2003-US22077	20030714
AU 2003253925	A1	AU 2003-253925	20030714

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003253925	A1 Based on	WO 2004009015

PRIORITY APPLN. INFO: US 2002-417999P 20021011; US 2002-396603P 20020718

INT. PATENT CLASSIF.:
MAIN: A61K000-00

BASIC ABSTRACT:

WO2004009015 A UPAB: 20040324

NOVELTY - Composition (A) comprises a neuropeptide Y (NPY) antagonist and an antiobesity agent or its salt or ester.

DETAILED DESCRIPTION - Composition (A) comprises a neuropeptide Y antagonist of formula (I) or (II) or their salts or esters and an antiobesity agent comprising a 5-hydroxytryptamine (HT) transporter inhibitor, norepinephrine (NE) transporter inhibitor, cannabinoid (CB) 1 antagonist/inverse agonist, Ghrelin antagonist, histamine receptor 3 (H3) antagonist/inverse agonist, melanin-concentrating hormone (MCH)1R antagonist, MCH2R agonist/antagonist, NPY1 antagonist, leptin, leptin derivatives, opioid antagonist, orexin antagonist, bombesin-like receptor (BRS) 3 agonist, cholecystokinin (CCK)-A agonist, ciliary neurotrophic factor (CNTF), CNTF derivatives, **growth hormone secretagogue** (GHS) agonist, 5HT2C agonist, monoamine reuptake inhibitor, uncoupling protein (UCP) -1, 2, and 3 activator, beta 3 agonist, thyroid hormone beta agonist, phosphodiesterase (PDE) inhibitor, fatty acid synthase (FAS) inhibitor, diacylglycerol acyltransferase (DGAT2) inhibitor, acetyl-coenzyme-A carboxylase-2 (ACC2) inhibitor, glucocorticoid antagonist, acyl-estrogens, lipase inhibitor, fatty acid transporter inhibitor, dicarboxylate transporter inhibitor, glucose transporter inhibitor, serotonin reuptake inhibitors, metformin or topiramate.

Ar1 = aryl or heteroaryl (both optionally substituted by halo, NO2, lower alkyl, halo(lower)alkyl, hydroxy(lower)alkyl, cyclo(lower)alkyl, lower alkenyl, lower alkoxy, halo(lower)alkoxy, lower alkylthio, carboxyl, lower alkanoyl, lower alkoxycarbonyl, lower alkylene optionally substituted by oxo or Q-Ar2);

Ar2 = aryl or heteroaryl (both optionally substituted by halo, CN, lower alkyl, halo(lower)alkyl, hydroxy(lower)alkyl, OH, lower alkoxy, halo(lower)alkoxy, lower alkylamino, di-lower alkylamino, lower alkanoyl or aryl;

n = 0-1;

Q = a single bond or carbonyl;

T, U, V, W = N or methine (optionally substituted by halo, lower alkyl, OH or lower alkoxy);

X = N or methine, and
Y = imino (optionally substituted by lower alkyl) or O,
provided that at least two of T, U, V and W are methine.
An INDEPENDENT CLAIM is also included for a composition (B) comprising an NPY5 agonist and a melanocortin receptor 4 (MC4R) agonist.
ACTIVITY - Anorectic; Eating-Disorders-Gen.; Hypotensive; Antidiabetic; Antilipemic; Cytostatic; Antiarthritic; Osteopathic; CNS-Gen.; Hepatotropic; Litholytic; Cardiant; Antiarrhythmic; Gynecological; Endocrine-Gen.
Tests are described, but no results are given.
MECHANISM OF ACTION - NYP antagonist; MC4R agonist.
USE - Useful to prevent obesity and to treat obesity or related disorders (preferably overeating, bulimia, hypertension, diabetes, elevated plasma insulin concentrations, insulin resistance, dyslipidemia, hyperlipidemia, endometrial, breast, prostate and colon cancer, osteoarthritis, obstructive sleep apnea, cholelithiasis, gallstones, coronary heart disease, abnormal heart rhythms, heart arrhythmias, myocardial infarction, polycystic ovarian disease, craniopharyngioma, the Prader-Willi Syndrome, Frohlich's syndrome, GH-deficient subjects, normal variant short stature, Turner's syndrome and acute lymphoblastic leukemia) associated with excessive food intake (all claimed), and to maintain weight loss.
ADVANTAGE - The combination of an NPY5 antagonist and an anti-obesity agent that decreases appetite or food intake, increases the metabolic rate or inhibits nutrient absorption, is advantageous in the treatment of obesity over treatment with either the NPY5 antagonist or the antiobesity agent alone. The compositions allow the use of the maximum efficacious dose of a NPY5 antagonist, which has no significant side effects, and a sub-clinical dose of a second antiobesity agent, with known side effects, resulting in effective treatment with fewer side effects than current monotherapies.
Dwg.0/5

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B01-A01; B04-A01; B04-H01; B04-L05; B06-A02; B06-A03; B06-D03; **B07-D03**; B07-D04; B07-D05; B07-E01; B10-A12C; B10-A17; B10-B03B; B10-B04B; B14-C09; B14-E11; B14-F01; B14-F01A; B14-F02B; B14-F06; B14-H01; B14-N01; B14-N12; B14-N14; B14-S04; C01-A01; C04-A01; C04-H01; C04-L05; C06-A02; C06-A03; C06-D03; **C07-D03**; C07-D04; C07-D05; C07-E01; C10-A12C; C10-A17; C10-B03B; C10-B04B; C14-C09; C14-E11; C14-F01; C14-F01A; C14-F02B; C14-F06; C14-H01; C14-N01; C14-N12; C14-N14; C14-S04

TECH UPTX: 20040324
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Compounds: The antiobesity agent is an acyl-estrogen (preferably an oleoyl-estrone), a CB-1 antagonist/inverse agonist (preferably rimonabant), an opioid antagonist (preferably nalmefene), a monoamine reuptake inhibitor (preferably sibutramine), a lipase inhibitor (preferably orlistat), leptin, CNTF, CNTF derivatives (preferably axokine), metformin or topiramate. The antiobesity agent is also aminorex, amphechloral, amphetamine, benzphetamine, chlorphentermine, clobenzorex, cloforex, clominorex, clortermine, cyclexedrine, dexfenfluramine, dextroamphetamine, diethylpropion, diphemethoxidine, N-ethylamphetamine, fenbutrazate, fenfluramine, fenisorex, fenproporex, fludorex, fluminorex, furfurylmethylamphetamine, levamfetamine, levophacetoperane, mazindol, mefenorex, metamfepramone, methamphetamine, norpseudoephedrine, pentorex, phendimetrazine, phenmetrazine, phentermine, phenylpropanolamine, picilorex or zona amide.

The NPY5 antagonist is administered as a combined preparation simultaneously, separately or sequentially with the antiobesity agent or the MC4R agonist.
The NPY5 antagonist is one of 107 specific compounds, especially 3-oxo-N-(5-phenyl-2-pyrazinyl)-spiro(isobenzofuran-1(3H),4'-piperidine)-1'-carboxamide, 3-oxo-N-(7-trifluoromethylpyrido(3,2-b)pyridin-2-yl)spiro-(isobenzofuran-1(3H),4'-piperidine)-1'-carboxamide, N-(5-(3-fluorophenyl)-2-pyrimidinyl)-3-oxospiro-(isobenzofuran-1(3H),4'-piperidine)-1'-carboxamide, trans-3'-oxo-N-(5-phenyl-2-pyrimidinyl)spiro(cyclohexane-1,1'(3'H)-isobenzofuran)-4-carboxamide, trans-3'-oxo-N-(1-(3-quinolyl)-4-imidazolyl)spiro(cyclohexane-1,1'(3'H)-isobenzofuran)-4-carboxamide, trans-3-oxo-N-(5-phenyl-2-pyrazinyl)spiro(4-azaiso-benzofuran-1(3H),1'-cyclohexane)-4'-carboxamide, trans-N-(5-(3-fluorophenyl)-2-pyrimidinyl)-3-oxospiro(5-azaisobenzofuran-1(3H),1'-cyclohexane)-4'-carboxamide, trans-N-(5-(2-fluorophenyl)-2-pyrimidinyl)-3-oxospiro(5-azaisobenzofuran-1(3H),1'-cyclohexane)-4'-carboxamide, trans-N-(1-(3,5-difluorophenyl)-4-imidazolyl)-3-oxospiro(7-azaisobenzofuran-1(3H),1'-cyclohexane)-4'-carboxamide, trans-3-oxo-N-(1-phenyl-4-pyrazolyl)spiro(4-azaisobenzofuran-1(3H),1'-cyclohexane)-4'-carboxamide, trans-N-(1-(2-fluorophenyl)-3-pyrazolyl)-3-oxospiro(6-azaisobenzofuran-1(3H),1'-cyclohexane)-4'-carboxamide, trans-3-oxo-N-(1-phenyl-3-pyrazolyl)spiro(6-azaisobenzofuran-1(3H),1'-cyclohexane)-4'-carboxamide or trans-3-oxo-N-(2-phenyl-1,2,3-triazol-4-yl)spiro(6-azaisobenzofuran-1(3H),1'-cyclohexane)-4'-carboxamide.

ABEX UPTX: 20040324

ADMINISTRATION - The dosage is 0.0001-100 (preferably 0.001-50) mg/kg/day of each component, orally or intravenously.

EXAMPLE - None given.

L115 ANSWER 17 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-279996 [26] WPIX
CROSS REFERENCE: 1998-583196 [49]; 2000-465955 [40]; 2000-465956 [40]; 2001-112312 [12]; 2001-520042 [57]; 2002-082942 [11]; 2003-810559 [76]; 2003-810569 [76]; 2004-030477 [03]; 2004-050510 [05]; 2004-118578 [12]; 2004-130196 [13]; 2004-141375 [14]; 2004-141427 [14]; 2004-153869 [15]; 2004-223910 [21]; 2004-236464 [22]; 2004-345154 [32]
DOC. NO. CPI: C2004-107955
TITLE: Use of a peptide for inhibiting binding of insulin-like growth factor binding protein 3 to insulin-like growth factor-1 (IGF-I) or for increasing serum and tissue levels of biologically active IGF-1 in a mammal.
DERWENT CLASS: B04
INVENTOR(S): CLARK, R G; LOWMAN, H B; ROBINSON, I C A F
PATENT ASSIGNEE(S): (GETH) GENENTECH INC
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 6713451	B1	20040330	(200426)*		183	A61K038-10

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6713451	B1 CIP of	US 1997-825852	19970404
	Div ex	US 1998-52888	19980331
		US 2000-724062	20001128

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 6713451	B1 CIP of	US 6121416
	Div ex	US 6251865

PRIORITY APPLN. INFO: US 1998-52888 19980331; US
1997-825852 19970404; US
2000-724062 20001128
INT. PATENT CLASSIF.:
MAIN: A61K038-10
SECONDARY: A61K038-27; A61K038-28; C07K007-08; C07K014-62
BASIC ABSTRACT:
US 6713451 B UPAB: 20040520
NOVELTY - Use of a peptide for inhibiting binding of insulin-like growth factor protein 3 (IGFBP-3) to IGF-I or for increasing serum and tissue levels of biologically active IGF-1 in a mammal, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) inhibiting binding of IGFBP-3 to IGF-I in a mammal; and
(2) increasing serum and tissue levels of biologically active IGF-I in a mammal.
ACTIVITY - Antidiabetic; Anorectic; Neuroprotective; Cardiant; Cardiovascular-Gen.; Nephrotropic; Immunomodulator.
No biological data given.
MECHANISM OF ACTION - Inhibitor of binding of insulin-like growth factor binding protein 3 to insulin-like growth factor 1.
USE - The peptide is useful for inhibiting binding of IGFBP-3 to IGF-I or for increasing serum and tissue levels of biologically active IGF-1 in a mammal. It is also useful for treating hypoglycemic, obesity-related, neurological, cardiac, anabolic, renal, or immunologic disorder.
Dwg.0/44
FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: B04-C01C; B04-H06H; B04-J03A; **B07-D03**; B07-D09; B10-B02D; B14-E12; B14-F01; B14-F02; B14-F10; B14-G03; B14-J01; B14-N10
TECH UPTX: 20040421
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: Inhibiting binding of IGFBP-3 to IGF-I in a mammal comprises administering to the mammal an amount of a peptide that inhibits binding of IGFBP-3 to IGF-I, where the peptide comprises 12 amino acids (SEQ ID NO. 108). The method further comprises administering to the mammal a **growth hormone**, a **growth hormone** releasing peptide, a **growth hormone** releasing **hormone**, a **growth hormone secretagogue**, an insulin-like growth factor (IGF), an IGF in combination with an IGF binding protein, an IGF binding protein (IGFBP), insulin, or a hypoglycemic agent. The mammal is human, which is afflicted with a hypoglycemia, obesity-related, neurological, cardiac, anabolic, renal or immunologic disorder. Increasing serum and tissue levels of biologically active IGF-I in a mammal comprises administering to the mammal an amount of a peptide that binds IGFBP-3 to reduce plasma insulin secretion when administered to a mammal.
ABEX UPTX: 20040421
SPECIFIC SEQUENCES - Specifically claimed is a peptide comprising 12 amino acids (SEQ ID NO. 108), fully defined in the specification.

ADMINISTRATION - Dosage is 10-200 microgram/kg/day. Administration can be

through parenteral routes.

EXAMPLE - No relevant example given.

L115 ANSWER 18 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-062141 [06] WPIX
DOC. NO. CPI: C2004-025452
TITLE: New fluorinated cyclic amide compounds are dipeptidyl peptidase-IV inhibitors used for treating e.g. diabetes type 1 and 2, obesity, osteoporosis, ulcer, hypertension, atherosclerosis, cataracts, anxiety, depression and insomnia.
DERWENT CLASS: B03
INVENTOR(S): HULIN, B; PARKER, J C
PATENT ASSIGNEE(S): (PFIZ) PFIZER INC; (PFIZ) PFIZER PROD INC
COUNTRY COUNT: 103
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2003101958	A2	20031211	(200406)*	EN	36	C07D207-00
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW						
US 6710040	B1	20040323	(200421)			C07D205-04
US 2004132713	A1	20040708	(200445)			A61K031-397
AU 2003232405	A1	20031219	(200449)			C07D207-00

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003101958	A2	WO 2003-IB2257	20030523
US 6710040	B1 Provisional	US 2002-386157P	20020604
		US 2003-455734	20030603
US 2004132713	A1 Provisional	US 2002-386157P	20020604
	Cont of	US 2003-455734	20030603
		US 2003-742657	20031219
AU 2003232405	A1	AU 2003-232405	20030523

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 2004132713	A1 Cont of	US 6710040
AU 2003232405	A1 Based on	WO 2003101958

PRIORITY APPLN. INFO: US 2002-386157P 20020604; US 2003-455734 20030603; US 2003-742657 20031219
INT. PATENT CLASSIF.:
MAIN: A61K031-397; C07D205-04; C07D207-00
SECONDARY: A61K031-40; A61K031-401; A61K031-445; C07D207-04; C07D211-06; C07D211-60
BASIC ABSTRACT:
WO2003101958 A UPAB: 20040123

NOVELTY - Fluorinated cyclic amide compounds (I), are new.

DETAILED DESCRIPTION - Fluorinated cyclic amides of formula H2N-CH(R2)-COR1(I), their salts and prodrugs are new.

R1 = 3-fluoroazetidin-1-yl, 3,3-difluoroazetidin-1-yl, 3,4-difluoropyrrolidin-1-yl, 3,3,4-trifluoropyrrolidin-1-yl, 3,3,4,4-tetrafluoropyrrolidin-1-yl, 3-fluoropiperidin-1-yl, 4-fluoropiperidin-1-yl, 3,4-difluoropiperidin-1-yl, 3,5-difluoropiperidin-1-yl, 3,3-difluoropiperidin-1-yl, 4,4-difluoropiperidin-1-yl, 3,4,5-trifluoropiperidin-1-yl, 3,3,4-trifluoropiperidin-1-yl, 3,3,5-trifluoropiperidin-1-yl, 3,4,4-trifluoropiperidin-1-yl, 3,3,4,5-tetrafluoropiperidin-1-yl, 3,4,4,5-tetrafluoropiperidin-1-yl, 3,3,4,4-tetrafluoropiperidin-1-yl, 3,3,5,5-tetrafluoropiperidin-1-yl, 3,3,4,5,5-pentafluoropiperidin-1-yl, 3,3,4,4,5-pentafluoropiperidin-1-yl or 3,3,4,4,5,5-hexafluoropiperidin-1-yl, and

R2 = 1-8C alkyl or 3-8C cycloalkyl.

INDEPENDENT CLAIMS are also included for

(1) a composition which comprises (I) and a second compound comprising insulin or its analog, insulinotropin, biguanide, alpha 2 antagonist or imidazoline, glitazone, aldose reductase inhibitor, glycogen phosphorylase inhibitor, sorbitol dehydrogenase inhibitor; fatty acid oxidation inhibitor; alpha -glucosidase inhibitor, beta -agonist, phosphodiesterase inhibitor, lipid-lowering agent, antiobesity agent; vanadate, vanadium complex or peroxovanadium complex, amylin antagonist, glucagon antagonist, **growth hormone secretagogue**, gluconeogenesis inhibitor, somatostatin analog, inhibitor of renal glucose, antilipolytic agent or salts or prodrugs of the second compound, and

(2) identifying an agent as a dipeptidyl peptidase (DPP-IV) inhibitor which comprises administering the agent to a fasted, diabetic KK/H1J mouse, subjecting the mouse to an oral glucose challenge, followed by the assessment of the response in the mouse to the challenge. The agent may be identified as a treatment for Type 2 diabetes, metabolic syndrome, hyperglycemia, impaired glucose tolerance, glucosuria, metabolic acidosis, cataracts, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, diabetic cardiomyopathy, Type 1 diabetes, obesity, a condition exacerbated by obesity, hypertension, hyperlipidemia, atherosclerosis, osteoporosis, osteopenia, frailty, bone loss, bone fracture, acute coronary syndrome, infertility due to polycystic ovary syndrome, to prevent diseases progression in Type 2 diabetes, anxiety, depression, insomnia, chronic fatigue, epilepsy, an eating disorder, chronic pain, alcohol addiction, a disease associated with intestinal motility, ulcer, irritable bowel syndrome, inflammatory bowel syndrome or short bowel syndrome.

ACTIVITY - Antidiabetic; Vasotropic; Ophthalmological; Neuroprotective; Nephrotropic; Cardiovascular-Gen.; Anorectic; Hypotensive; Antilipemic; Antiarteriosclerotic; Osteopathic; Antiinfertility; Gynecological; Muscular-Gen.; Immunomodulator; Anticonvulsant; Gastrointestinal-Gen; Antiulcer; Antiinflammatory; Tranquilizer; Antidepressant; Sedative; Eating-Disorders-Gen.; Analgesic; Antialcoholic; Cardiant.

MECHANISM OF ACTION - Dipeptidyl peptidase-IV inhibitor.

In an in vitro assay for dipetidyl peptidase inhibition measured as described in Assay of dipetidyl peptidase IV in serum by fluorometry of 4-methoxy-2-naphthylamide. (1988) Scharpe, S., Demeester, 1., Vanhoof, G., Hendriks., D., Van Sande, M., Van Camp, K. and Yaron, A,Clin.Chem.34:2299-2301; Dipeptidyl peptidases of human lymphocytes (1988) Lodja, Z-Czechoslovak Medicine, 11:181-194, results showed that (I) e.g. (2S,3S)-2-amino-3-methyl-1-(3,3,4,4-tetrafluoropyrrolidin-1-yl)-pentan-1-one exhibited a median inhibitory concentration (IC50) of upto 3 mu M.

USE - Used for treating Type 2 diabetes, metabolic syndrome,

hyperglycemia, impaired glucose tolerance, glucosuria, metabolic acidosis, cataracts, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, diabetic cardiomyopathy, Type 1 diabetes, obesity, a condition exacerbated by obesity, hypertension, hyperlipidemia, atherosclerosis, osteoporosis, osteopenia, frailty, bone loss, bone fracture, acute coronary syndrome, infertility due to polycystic ovary syndrome, disease progression in Type 2 diabetes, chronic fatigue, epilepsy, disease associated with intestinal motility, ulcer, irritable bowel syndrome, inflammatory bowel syndrome, anxiety, depression, insomnia, an eating disorder, chronic pain and alcohol addiction (all claimed).

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B07-D01; **B07-D03**; B07-D05; B14-C01; B14-C03; B14-D01B; B14-D01C; B14-E04; B14-E08; B14-E10; B14-F01; B14-F02; B14-F06; B14-F07; B14-F09; B14-J01A1; B14-J01A2; B14-J01B4; B14-J07; B14-M01A; B14-N03; B14-N10; B14-P02; B14-S04

TECH UPTX: 20040123

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: No general preparation of (I) is given.

ABEX UPTX: 20040123

SPECIFIC COMPOUNDS - 19 compounds (I) are specifically claimed e.g: (2S,3S)-2-amino-3-methyl-1-(3,3,4,4-tetrafluoropyrrolidin-1-yl)-pentan-1-one hydrochloride (Ia).

ADMINISTRATION - Dosage of (I) is 0.01-30 (preferably 0.01-1) mg/kg/day in single or divided doses by oral, parenteral or intranasal administration.

EXAMPLE - 1-(-3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (319 mg) was added to a mixture of (L)-Boc-isoleucine (322 mg), 3,3,4,4-tetrafluoropyrrolidine hydrochloride (300 mg), hydroxybenzotriazole (225 mg), and triethylamine (0.23 ml) in dichloromethane (10 ml) and the mixture was worked up to give ((1S, 2S)-2-methyl-1-(3,3,4,4-tetrafluoropyrrolidine-1-carbolidine-1-carbonyl)-butyl)-carbamic acid tert ester (415 mg, 86%). This compound (200 mg) was dissolved in ethyl acetate (4 ml), cooled to 0degreesC, treated with gaseous hydrochloric acid and the mixture was worked up to give (2S,3S)-2-amino-3-methyl-1-(3,3,4,4-tetrafluoropyrrolidin-1-yl)-pentan-1-one hydrochloride (Ia) (124 mg; 76%).

L115 ANSWER 19 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-081888 [08] WPIX
DOC. NO. CPI: C2004-033654
TITLE: Pharmaceutical composition having androgen receptor modulatory activity, useful for the treatment of muscular dystrophy, sarcopenia, depression and nervousness comprises imidazol derivatives.
DERWENT CLASS: B02
INVENTOR(S): AUGERI, D; BI, Y; HAMANN, L; HOLUBEC, A; HUANG, Y; ROBL, J; SIMPKINS, L; SUN, C; WANG, T; LI, J J; SUTTON, J C
PATENT ASSIGNEE(S): (BRIM) BRISTOL-MYERS SQUIBB CO; (AUGE-I) AUGERI D; (BIYY-I) BI Y; (HAMA-I) HAMANN L; (HOLU-I) HOLUBEC A; (HUAN-I) HUANG Y; (ROBL-I) ROBL J; (SIMP-I) SIMPKINS L; (SUNC-I) SUN C; (WANG-I) WANG T; (LIJJ-I) LI J J; (SUTT-I) SUTTON J C
COUNTRY COUNT: 103
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2003096980	A2	20031127	(200408)*	EN	176	A61K000-00
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW						
US 2004019063	A1	20040129	(200413)			A61K031-519
AU 2003234609	A1	20031202	(200442)			A61K000-00
US 2004181064	A1	20040916	(200461)			C07D471-02

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003096980	A2	WO 2003-US15375	20030515
US 2004019063	A1 Provisional	US 2002-381616P	20020517
	Provisional	US 2002-406711P	20020829
		US 2003-438722	20030515
AU 2003234609	A1	AU 2003-234609	20030515
US 2004181064	A1 Provisional	US 2002-381616P	20020517
	Provisional	US 2002-406711P	20020829
	CIP of	US 2003-438722	20030515
		US 2004-780415	20040217

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003234609	A1 Based on	WO 2003096980

PRIORITY APPLN. INFO: US 2002-406711P 20020829; US 2002-381616P 20020517; US 2003-438722 20030515; US 2004-780415 20040217

INT. PATENT CLASSIF.:
MAIN: A61K000-00; A61K031-519; C07D471-02
SECONDARY: A61K031-4188

BASIC ABSTRACT:

WO2003096980 A UPAB: 20040202

NOVELTY - Pharmaceutical composition (A) capable of modulating the androgen receptor comprises imidazol derivatives (I).

DETAILED DESCRIPTION - Pharmaceutical composition (A) capable of modulating the androgen receptor comprises imidazol derivatives of formula (I).

R1 = H, (substituted) alkyl, (substituted) alkenyl, (substituted) arylalkyl, CO2R4, CONR4R4' or CH2OR4; either

R2, R2' = H, (substituted) alkyl, OR3, SR3, halo, NH(CO)R4, NHCO2R4, NHCONR4R4' or NHSO2R4; or

R2,R2' = H or alkyl, with the exception that R2 and R2' can both be OR3 when R3 is not H;

R3 = H, (substituted) alkyl, CHF2, CF3 and COR4;

R4, R4' = T;

R5, R5' = T with at least one of R5, R5' being H or R5 and R5' form a double bond with O, S, NR7 or CR7R7';

R6, R6' = T with at least one of R6 and R6' being H or R6 and R6' form a double bond with O, S , NR7 or CR7R7';

R7, R7' = T or OR4 ;
G = aryl, heterocyclo or heteroaryl group (mono or polycyclic), optionally substituted with halo, CN, CF3, OR4, CO2R4, NR4R4', CONR4R4', CH2OR4 or T ;
T = H, (substituted) alkyl, (substituted) alkenyl, (substituted) alkynyl, (substituted) cycloalkyl, (substituted) arylalkyl, (substituted) aryl or (substituted) heteroaryl;
W = (CR6R6'), C(R6)OR3, C(R6)(NR4R4'); and
n = 1-2;
Provided that:
(1) when R5 and R5' and/or R6 and R6' form a double bond with CR7R7', either R7 or R7' is OR4 and R4 is not H;
(2) excluding compounds where the following occurs simultaneously;
(a) R2, R2' = H, OR3, halo, NHCOR4, NHCO2R4, NHCONR4R4' or NHSO2R4;
(b) R5, R5' = H or form a double bond with O or S;
(c) R6, R6' = T, where at least one of R6 and R6' is H or R6 and R6' taken together form a double bond with O, S or NR7;
(d) R7 = T; and
(e) R13 = H, CN, NO2, halo, heterocyclo, OR14, CO2R15, CONHR15, COR15, S(O),R15, SO2NR-15R15', NHCOR15 and NHSO2R15;
(f) R14 = H, alkyl or substituted alkyl, CHF2, CF3 and COR15;
(g) R15 and R15' = T or CN; A,B = H, halo, CN, NO2, (substituted) alkyl or OR14; and
(h) p = 0-2.
INDEPENDENT CLAIMS are also included for
(a) a compound of formula (Ib);
(b) preparation of a compound of formula (Id);
(c) preparation of a compound of formula (Ie);
(d) preparation of a compound of formula (XII); and
(e) preparation of a compound of formula (XIV).
X,Y = O or S.
ACTIVITY - Muscular-Gen.; Antilipemic; Immunomodulator; Antidepressant; Eating-disorder-Gen.; Tranquilizer; Analgesic; Antianginal; Antidiabetic; Anorectic; Osteopathic; Endocrine-Gen.; Nootropic; Contraceptive.
MECHANISM OF ACTION - Androgen receptor modulator.
USE - (I) is useful for the treatment or delaying the progression or onset of muscular atrophy, lipodystrophy, long-term critical illness, sarcopenia, frailty or age-related functional decline, reduced muscle strength and function, reduced bone density or growth, the catabolic side effects of glucocorticoids, chronic fatigue syndrome, bone fracture repair, acute fatigue syndrome and muscle loss following elective surgery, cachexia, chronic catabolic state, eating disorders, side effects of chemotherapy, wasting, depression, nervousness, irritability, stress, growth retardation, reduced cognitive function, male contraception, hypogonadism, Syndrome X, diabetic complications and obesity (claimed).
ADVANTAGE - (I) have good specificity for one or more steroid receptors that have reduced or no cross-reactivity for other steroid or intracellular receptors, which is of significant value in the treatment of male and female hormone-responsive diseases. (I) are selective modulators of the steroid binding receptors, particularly non-steroidal, non-toxic tissue selective androgen receptor modulators that activate the androgen receptor in the skeletal muscle with limited or neutral effect on other androgen responsive tissues.
Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B06-D05; B06-D07; **B07-D03**; B07-D05; B14-C03; B14-D01A; B14-D02; B14-E11; B14-E12; B14-F01D; B14-J01A1; B14-J01A4; B14-J01B4; B14-J05;

B14-N01; B14-N07; B14-P01A

TECH UPTX: 20040202

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (claimed)
(a) preparation of 1,3-dioxopyrrolo-imidazol compound (Id) comprises the hydrolysis of aceto-amido imidazol compound (IVa) under basic conditions to give amido-imidazol derivative (XIX) which is then carried on to a compound (Id) with the use of a coupling reagent;
(b) preparation of 3-oxopyrrolo imidazol compound (Ie) comprises optionally protecting the compound (IVa; R2 = OH) with protecting group by treatment with a silylating reagent and then reducing with a reducing agent to give amido-alcoholic imidazol-derivative (XX) which is then derivatized with a leaving group and p-toluene sulfonyl chloride and then treated with a base to give (Ie);
(c) amine-imidazol compounds of formula (XII) prepared by reacting an aldehyde of formula (IX) with an amine of formula (XV) in the presence of reducing agent to give (XII); and
(d) 3-oxo pyrrolo-imidazol compound of formula (XIV) is prepared by subjecting (XII) to N-deprotection to produce an amine-imidazol compound of formula (XIII) and reacting (XIII) with phosgene or a phosgene equivalent in the presence of base to form (XIV).
Preferred Components: Protecting group is tert-butyldimethylsilyl and the silylating reagent is t-butyldimethylsilyl (chloride). Reducing agent is lithium aluminum hydride or lithium borohydride. Leaving group is tosyl and the base is potassium tert-butoxide.
Preferred Composition: (A) further comprises a growth promoting agent and comprises one additional therapeutic agent such as parathyroid hormone, bisphosphonates, estrogen, testosterone, progesterone, selective estrogen receptor modulators, **growth hormone secretagogues**, **growth hormone**, progesterone receptor modulators, anti-diabetic agents, anti-hypertensive agents, anti-inflammatory agents, anti-osteoporosis agents, anti-obesity agents, cardiac glycosides, cholesterol lowering agents, anti-depressants, anti-anxiety agents, anabolic agents, and thyroid mimetics.

ABEX UPTX: 20040202

SPECIFIC COMPOUNDS - The use of 2-methyl-4-((7s, 7aR)-7-hydroxy-3-oxotetra-hydro-1H-pyrrolo-(1,2-C) imidazol-2-(3H)-yl)-3-methyl benzonitrile (Ia), 2-methyl-4-((7s, 7aR)-7-hydroxy-3-oxotetra-hydro-1H-pyrrolo-(1,2-C) imidazol-2-(3H)-yl)-3-chloro benzonitrile, 2-methyl-4-((7s, 7aR)-7-hydroxy-3-oxotetra-hydro-1H-pyrrolo-(1,2-C) imidazol-2-(3H)-yl)-3-cyano benzonitrile, 2-methyl-4-((7s, 7aR)-7-hydroxy-3-oxotetra-hydro-1H-pyrrolo-(1,2-C) imidazol-2-(3H)-yl)-3-chloro bromo benzene, 2-methyl-4-((7s, 7aR)-7-hydroxy-3-oxotetra-hydro-1H-pyrrolo-(1,2-C) imidazol-2-(3H)-yl)-3-fluoro benzonitrile is specifically claimed as (I).

ADMINISTRATION - Dosage is 0.01-2000 mg/day by oral, sublingual, buccal, parenteral, topical, rectal, liposomal administration or by inhalation. (I) is administered concurrently or sequentially (claimed).

EXAMPLE - To a solution of methyl-(28, 35)-1-(((3-chloro-4-cyano-2-methylphenyl)amino)-carbonyl)-3-(tert-butyl-dimethyl silanyloxy-pyrrolidine-2-carboxylate (300 mg) in anhydrous tetrahydrofuran (THF) (6.7 ml) at -25 degrees C was added 1 N lithium aluminum hydride in THF (1.34 ml) for 10 minutes. The solution was then warmed to 0 degrees C and stirred for 2 hours. The mixture was worked up to give (2R, 3S)-N-(3-chloro-4-cyano-2-methylphenyl)3-tert-butyldimethylsilanyloxy-2-(hydroxymethyl) pyrrolidine -1- carboxamide (i) (78%). A solution of (i) (150 mg) in anhydrous THF (4.8 ml) at 0 degrees C was treated with 97% tert-potassium butoxide and stirred at 0 degrees C for 5 min. To the solution was added a solution of toluenesulfonyl chloride (81.6 mg) in anhydrous THF, and was stirred at 0 degrees C. The mixture was worked up

to give 2-Chloro-4-((7S, 7aR)-7-(tert-butyldimethylsilanyloxy)-3-oxo-tetrahydro-1H-pyrrolo (1,2C) imidazol-2-(3H) ylmethylbenzonitrile (ii) (90%). To a solution of (ii) (112.4 mg) in anhydrous THF (5.0 ml) at 0 degrees C was added 1M tetrabutylammonium fluoride in THF (0.32 ml). The solution was stirred at 0 degrees C for 10 minutes at room temperature for 19 hours. The mixture was worked up give 2-Chloro-4-((7S, 7aR)-7-hydroxy-3-oxotetrahydro-1H-pyrrolo (1,2-c) imidazol-2-(3H)-yl)-3-methylbenzonitrile (Ia) (95%).

DEFINITIONS - Preferred Definition:
G = formula (a)-(d);
R8, R9, R10, R11 = H, NO2, CN, CF3, OR4, CO2R4, NR4R4', CONR4R4', CH2OR4, (substituted) alkyl, (substituted) alkenyl, (substituted) alkynyl, (substituted) cycloalkyl, (substituted) arylalkyl, (substituted) aryl or (substituted) heteroaryl;
A, F' = N or CR9;
J, K', L, P', Q = bond or R1;
R1 = H or alkyl;
R2, R2' = OH;
R5, R5' = H or form a double bond with O or S;
R6, R6' = forms a double bond with O or S; and
R8 = CN.

L115 ANSWER 20 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-180141 [17] WPIX
DOC. NO. CPI: C2004-071104
TITLE: New 4-azasteroid derivatives are tissue-selective androgen receptor modulators useful for the treatment of conditions caused by androgen deficiency e.g. osteoporosis, bone damage, obesity, prostate cancer and atherosclerosis.
DERWENT CLASS: B01
INVENTOR(S): MCVEAN, C A; WANG, J
PATENT ASSIGNEE(S): (MERI) MERCK & CO INC
COUNTRY COUNT: 102
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2003092588	A2	20031113	(200417)*	EN	181	A61K000-00
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW						
AU 2003223754	A1	20031117	(200442)			A61K000-00

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003092588	A2	WO 2003-US13120	20030425
AU 2003223754	A1	AU 2003-223754	20030425

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 2003223754 A1 Based on WO 2003092588

PRIORITY APPLN. INFO: US 2002-376779P 20020430
INT. PATENT CLASSIF.:
MAIN: A61K000-00
BASIC ABSTRACT:
WO2003092588 A UPAB: 20040310
NOVELTY - 4-azasteroid derivatives (I) and their salts and enantiomers are new.

DETAILED DESCRIPTION - 4-azasteroid derivatives of formula (I) and their salts and enantiomers are new.

n = 0-2;

A1 - B1 = CH=CH or CH2CH2;

c = a double bond; either

R1 = H, OH, 1-4C alkoxy, hydroxymethyl or 1-3C alkyl (optionally substituted with 1-7F); and

R4 = halo, 1-6C alkyl (optionally substituted with 1-3 of CN, carboxy, halo, OH, oxo, 1-4C alkoxy or 1-4C alkylthio), 2-6C alkenyl, 2-6C alkynyl, (CH2)n-phenyl or (CH2)n-naphthyl; or

CR4 = carbonyl or cyclopropyl; and

c = a single bond; or

R1R4 together with the atoms to which they are attached = 5- or 6-membered ring (optionally containing an additional heteroatom of O, S or N1-4C alkyl); either

R2 = H or 1-4C alkyl; and

R3 = 1-4C alkyl (optionally substituted by halo, OH, 1-4C alkoxy and/or 1-4C alkylamino) or A-T); or

R2R3 form a 5- or 6-membered saturated ring fused with a 5- or 6-aromatic ring system having 0-2 heteroatoms of N, O or S; A = (CH2)n (either optionally substituted by either 1-2 of halo, OH or 1-4C alkyl or by two substituents on the same (CH2) atom, together with the C atom to which they are attached forming a cyclopropyl group); and T = phenyl, naphthyl, benzimidazolyl, benzofuranyl, benzothiophenyl, benzoxazolyl, benzothiazolyl, benzodihydrofuranyl, 1,3-benzodioxolyl, 2,3-dihydro-1,4-benzodioxinyl, indolyl, quinolyl, isoquinolyl, furanyl, thienyl, imidazolyl, oxazolyl, thiazolyl, isoxazolyl, isothiazolyl, pyrazolyl, pyrrolyl, pyridyl, pyrimidyl, pyrazinyl, thiadiazolyl, oxadiazolyl, triazolyl, imidizopyridinyl, tetrazolyl or indanyl (optionally substituted by 1-3 of halo, phenyl, 1-8C alkyl, 3-8C cycloalkyl, 3-8C cycloheteroalkyl, phenyl(1-6C alkyl), amino(0-6C alkyl), (1-6C alkylamino)0-6C alkyl, (1-6C alkyl)2amino(0-6C alkyl), phenyl(0-6C alkylamino)0-6C alkyl, ((phenyl(0-6C alkyl))2amino(0-6C alkyl), 1-6C alkylthio, phenyl(0-6C alkylthio), 1-6C alkylsulfinyl, phenyl-0-6C alkylsulfinyl, 1-6C alkylsulfonyl, phenyl(0-6C alkylsulfonyl), 1-6C alkoxy(0-6C alkyl), phenyl(0-6C alkoxy)0-6C alkyl, hydroxycarbonyl(0-6C alkyl), 1-6C alkoxycarbonyl(0-6C alkyl), phenyl(0-6C alkoxycarbonyl)0-6C alkyl, hydroxycarbonyl(1-6C alkyloxy), hydroxy(0-6C alkyl), CN, NO2, perfluoro(1-4C alkyl), perfluoro(1-4C alkoxy), 1-6C alkylcarbonyloxy, phenyl(0-6C alkylcarbonyloxy), 1-6C alkylcarbonylamino, phenyl(0-6C alkylcarbonylamino), 1-6C alkylsulfonylamino, phenyl(0-6C alkylsulfonylamino), 1-6C alkoxycarbonylamino, phenyl(0-6C alkoxycarbonylamino), 1-6C alkylaminocarbonylamino, phenyl(0-6C alkylaminocarbonylamino), (1-6C alkyl)2 aminocarbonylamino, (phenyl(0-6C alkyl))2 aminocarbonylamino, (1-6C alkyl)2 aminocarbonyloxy and (phenyl(0-6C alkyl)2 aminocarbonyloxy, where the alkyl group is optionally substituted by 1-3 of halo, OH or 1-4C alkoxy).

INDEPENDENT CLAIMS are also included for

(a) a method for modulating a function mediated by the androgen receptor comprising administration of (I); and

(b) a method for activating the function of the androgen receptor

comprising administration of (I).

ACTIVITY - Osteopathic; Antiinflammatory; Dermatological; Endocrine-Gen; Antiarteriosclerotic; Antilipemic; Anorectic; Antianemic; Antiarthritic; Anti-HIV; Cytostatic; Immunomodulator; Muscular-Gen; Neuroprotective; Nootropic; Immunosuppressive; Gynecological.

MECHANISM OF ACTION - Androgen receptor modulator. Test details are described but no results given.

USE - (I) are tissue-selective androgen receptor (AR) modulators, functioning as AR agonists in bone/muscle tissue and as AR antagonists in the prostate or uterus. They are useful for treating conditions caused by androgen deficiency or which can be ameliorated by androgen replacement i.e. osteoporosis (preferred), osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, HIV-wasting, prostate cancer, cancer cachexia, muscular dystrophies, Alzheimer's disease, premature ovarian failure and autoimmune disease (claimed).

ADVANTAGE - Compounds (I) produce the positive response of androgen replacement therapy without the undesired side effects of non-tissue selective androgen receptor agonists, such as adverse effects on skin (acne and facial hair growth) and on lipid metabolism.

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B01-A01; B01-A02; B01-C05; B03-G; B03-J; B04-H06G; B04-H06H; B04-H06L; B04-J04A; B04-J04B; B05-A01B; B05-B01E; B05-B01F; B05-B01G; B06-A01; B06-D02; B06-D05; B06-D18; B07-A02B; B07-D02; **B07-D03** ; B07-D12; B10-B03B; B10-C04A; B14-C03; B14-C09; B14-D01A; B14-D01B; B14-D01C; B14-D02A; B14-D02A2; B14-D05D; B14-F06; B14-F07; B14-G02D; B14-H01; B14-L01; B14-L04; B14-L06; B14-N06B; B14-N14; B14-N17

TECH UPTX: 20040310

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: No general preparation is given.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: The function mediated by the androgen receptor is activated in bone and/or muscle tissue and blocked in the prostate or uterus. Treatment further comprises the administration of

(1) an estrogen or an estrogen derivative, alone or in combination with a progestin or progestin derivative (preferably conjugated estrogen, equine estrogen, 17beta-estradiol, estrone or 17beta-ethynyl estradiol (optionally in combination with 17beta-ethynyl estradiol with norethindrone and/or medroxyprogesterone acetate);

(2) a bisphosphonate i.e. alendronate (preferably alendronate monosodium hydrate or alendronate monohydrate), clodronate, etidronate, ibandronate, incadronate, minodronate, neridronate, olpadronate, pamidronate, piridronate, risedronate, tiludronate or zoledronate);

(3) an antiestrogen or a selective estrogen receptor modulator (preferably raloxifene, clomiphene, zuclomiphene, enclomiphene, nafoxidene, CI-680, CI-628, CN-55,945-27, Mer-25, U-11,555A7, U-100A, tamoxifen, lasofoxifene, toremifene, azorxifene, EM-800, EM-652, TSE 424, droloxifene, idoxifene or levormeloxifene);

(4) an alphavbeta3 integrin receptor antagonist;

(5) a cathepsin K inhibitor;

(6) an osteoclast vacuolar ATPase inhibitor;

(7) calcitonin (preferably salmon calcitonin administered as a nasal spray);
(8) parathyroid hormone (PTH) or its analog (preferably PTH subcutaneous injection, human PTH (1-84), human PTH (1-34) and other partial sequences, native or with substitutions);
(9) osteoprotegerin; (all preferred)
(10) an HMG-CoA reductase inhibitor (preferably lovastatin, simvastatin, dihydroxy-open acid simvastatin, pravastatin, fluvastatin, atorvastatin, cerivastatin, rosuvastatin, pitavastatin or nisvastatin);
(11) an antagonist of VEGF binding to osteoclast receptors;
(12) an activator of peroxisome proliferator-activated receptor gamma;
(13) a calcium receptor antagonist;
(14) a **growth hormone secretagogue**;
(15) human **growth hormone**;
(16) insulin-like growth factor (IGF I or IGF II alone or in combination with IGF binding protein 3);
(17) a p38 protein kinase inhibitor;
(18) bone morphogenetic protein (preferably BMP 2, BMP 3, BMP 5, BMP 6, BMP 7, TGF beta, and GDF5);
(19) an inhibitor of BMP antagonism;
(20) a prostaglandin derivative (preferably agonists of prostaglandin receptors EP1, EP2, EP4, FP and IP);
(21) a fibroblast growth factor i.e. aFGF or bFGF;
(22) vitamin D or vitamin D derivative (preferably natural vitamin D, 25-OH-vitamin D3, 1-mu,25(OH)2 vitamin D3, 1-mu-OH-vitamin D3, 1-mu-OH-vitamin D2, dihydrotachysterol, 26,27-F6-1-mu, 25(OH)2 vitamin D3, 19-nor-1-mu,25(OH)2 vitamin D3, 22-oxacalcitriol, calcipotriol, 1-mu,25(OH)2-16-ene-23-yne-vitamin D3 (Ro 23-7553), EB1089, 20-epi-1-mu,25(OH)2 vitamin D3, KH1060, ED71, 1-mu,24(S)-(OH)2 vitamin D3 and 1-mu,24(R)-(OH)2 vitamin D3);
(23) vitamin K or vitamin K derivative;
(24) ipriflavone;
(25) fluoride salts (preferably sodium fluoride or monosodium fluorophosphate); or
(26) dietary calcium supplement (preferably calcium carbonate, calcium citrate or natural calcium salts).

ABEX UPTX: 20040310

SPECIFIC COMPOUNDS - Approximately 400 compounds (I) are specifically claimed, e.g. N-(2-fluorophenyl)-4-methyl-6-methyl-3-oxo-4-aza-5alpha-androst-5-en-17beta-carboxamide (Ia).

ADMINISTRATION - Administration of (I) for adults is 0.01-1000 (preferably 0.1-200) mg 1-4 times daily. Administration may be oral, intranasal, transdermal, rectal, vaginal (as suppositories) or intravenous. For oral administration, the unit dose per tablet is 0.01-1000 (preferably 0.01-500) mg.

EXAMPLE - A mixture of 1-ethyl-3-(3-dimethylaminopropyl)carbodimide -hydrochloride (33.2 g), aza derivative (50.0 g), and 4-(dimethylamino)pyridine (1.9 g) in methanol (300 ml) was stirred for 24 hours. The mixture was concentrated, diluted with water (1000 ml) and filtered to give 3-oxo-4-aza-5alpha-androst-5-en-17beta-carboxylic acid methyl ester (A). Sodium hydride (1.3 g) was gradually added to a suspension of (A)(7.0 g) in 100 ml dry tetrahydrofuran and the reaction mixture stirred for 1 hour. Dimethylsulfate (10 ml) was added in one portion and the mixture was stirred overnight. Methanol (30 ml) was gradually added followed by water (500 ml) after stirring for 3 hours. The mixture was worked up to give 4-methyl-3-oxo-4-aza-5alpha-androst-5-en-17beta-carboxylic acid methyl ester (B). N-bromo succinamide (6.2 g) and benzoyl peroxide (0.1 g) were added to a suspension of (B) (11 g) in carbon tetrachloride (100 ml) and the reaction mixture was refluxed for 4

hours. The mixture was then worked up to give 6-bromo-4-methyl-3-oxo-4-aza-5alpha-androst-5-en-17beta-carboxylic acid methyl ester (C). A mixture of (C) (0.8 g), potassium carbonate (0.7 g), (palladium tetrakis (triphenyl phosphine)) (0.2 g) and trimethylboroxine (0.3 ml) in N,N-dimethylformamide (15 ml) was purged with nitrogen for 10 minutes and then heated at 100degreesC overnight. The reaction was quenched with saturated aqueous sodium bicarbonate and then water (200 ml). The mixture was worked up to give 4-methyl-6-methyl-3-oxo-4-aza-5alpha-androst-5-en-17beta-carboxylic acid methyl ester (D). Sodium hydroxide (0.5 g) in 5 ml water was added to a solution of (D)(1.9 g) in 1,4-dioxane (20 ml). The mixture was refluxed overnight, acidified with 3N hydrochloric acid, diluted with 50 ml water and worked up to give 4-methyl-6-methyl-3-oxo-4-aza-5alpha-androst-5-en-17beta-carboxylic acid.

DEFINITIONS - Preferred Definitions:
R1 = H or CH3 (preferably CH3);
R2 = H;
R3 = A-T;
n = 0-1; either R4 = 1-4C alkyl (preferably CH3); or
CR4 = cyclopropyl; and
T = phenyl, imidazopyridinyl, benzimidazolyl, benzothiophenyl, indolyl, quinolyl, isoquinolyl, thienyl, imidazolyl, thiazolyl, pyrazolyl, pyrrolyl, pyridyl, pyrimidyl, pyrazinyl, thiadiazolyl, triazolyl or indanyl (preferably phenyl, benzimidazolyl, benzothiophenyl, indolyl, pyrazolyl, pyrrolyl, pyridyl, pyrimidyl, pyrazinyl, thiadiazolyl, imidazopyridinyl and triazolyl)

L115 ANSWER 21 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-779083 [73] WPIX
DOC. NO. CPI: C2003-214521
TITLE: New fluorinated 4-azasteroid derivatives useful for treating a condition e.g. weakened muscle tone, osteoporosis, osteopenia, or glucocorticoid-induced osteoporosis.
DERWENT CLASS: B01 B05
INVENTOR(S): MEISSNER, R S; PERKINS, J J
PATENT ASSIGNEE(S): (MERI) MERCK & CO INC
COUNTRY COUNT: 103
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2003077919	A1	20030925	(200373)*	EN	48	A61K031-473
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW						
AU 2003218235	A1	20030929	(200432)			A61K031-473
EP 1485095	A1	20041215	(200482)	EN		A61K031-473
R: AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC NL PT RO SE SI SK TR						

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003077919	A1	WO 2003-US8277	20030307

AU 2003218235	A1	AU 2003-218235	20030307
EP 1485095	A1	EP 2003-714228	20030307
		WO 2003-US8277	20030307

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003218235	A1 Based on	WO 2003077919
EP 1485095	A1 Based on	WO 2003077919

PRIORITY APPLN. INFO: US 2002-363822P 20020313
INT. PATENT CLASSIF.:
MAIN: A61K031-473
SECONDARY: C07D221-18
BASIC ABSTRACT:
WO2003077919 A UPAB: 20040331
NOVELTY - Fluorinated 4-azasteroid derivative (I), its salt or enantiomers are new.
DETAILED DESCRIPTION - Fluorinated 4-azasteroid derivative of formula (I), its salt or enantiomers are new.
n = 0 - 2;
a-b = CF=CH, CHFCH2 or CF2CH2;
R1 = H, hydroxymethyl or 1-3C alkyl (optionally mono- to hepta-substituted by F);
R2 = H or 1-4C alkyl;
R3 = 1-4C alkyl, (CH2)n-cycloheteroalkyl or (CH2)n-T (where alkyl or cycloheteroalkyl is optionally mono- to tri-substituted by halo, OH, or 1-4C alkoxy; and any (CH2) is optionally mono- to di-substituted by halo, OH or 1-4C alkyl or two substituents on the same methylene group together with carbon forms cyclopropyl group); and
T = phenyl, naphthyl, benzimidazolyl, benzofuranyl, benzothiophenyl, benzoxazolyl, benzothiazolyl, benzodihydrofuranyl, 1,3-benzodioxolyl, 2,3-dihydro-1,4-benzodioxinyl, indolyl, quinolyl, isoquinolyl, furanyl, thienyl, imidazolyl, oxazolyl, thiazolyl, isoxazolyl, isothiazolyl, pyrazolyl, pyrrolyl, pyridyl, pyrimidyl, pyrazinyl, thiadiazolyl, oxadiazolyl, triazolyl, tetrazolyl or indanyl (all optionally mono- to tri-substituted by halo, phenyl, 1-8C alkyl, 3-8C cycloalkyl, 3-8C cycloheteroalkyl, phenyl-1-6C alkyl, amino-0-6C alkyl, 1-6C alkylamino-0-6C alkyl, (1-6C alkyl)2amino-0-6C alkyl, 1-6C alkylthio, phenyl-0-6C alkylthio, 1-6C alkylsulfinyl, phenyl-0-6C alkylsulfinyl, 1-6C alkylsulfonyl, phenyl-0-6C alkylsulfonyl, 1-6C alkoxy-0-6C alkyl, phenyl-0-6C alkoxy-0-6C alkyl, hydroxycarbonyl-0-6C alkyl, 1-6C alkoxycarbonyl-0-6C alkyl, phenyl-0-6C alkoxycarbonyl-0-6C alkyl, hydroxycarbonyl-1-6C alkyloxy, hydroxy-0-6C alkyl, CN, nitro, perfluoro-1-4C alkyl, perfluoro-1-4C alkoxy, oxo, 1-6C alkylcarbonyloxy, phenyl-0-6C alkylcarbonyloxy, 1-6C alkylcarbonylamino, phenyl-0-6C alkylcarbonylamino, 1-6C alkylsulfonylamino, phenyl-0-6C alkylsulfonylamino, 1-6C alkoxycarbonylamino, phenyl-0-6C alkoxycarbonylamino, 1-6C alkylaminocarbonylamino, phenyl-0-6C alkylaminocarbonylamino, (1-6C alkyl)2 aminocarbonylamino, (phenyl-0-6C alkyl)2-aminocarbonylamino, (1-6C alkyl)2aminocarbonyloxy, or (phenyl-0-6C alkyl)2aminocarbonyloxy); or
R2+R3 = 5 - 6 membered saturated ring fused with 5 - 6 membered aromatic ring system (optionally containing 1 or 2 N, O or S).
An INDEPENDENT CLAIM is also included for treatment of osteoporosis in a mammal comprising administering (I).
ACTIVITY - Osteopathic; Gynecological; Dermatological; Endocrine-Gen.; Antiarteriosclerotic; Antilipemic; Anorectic; Antianemic; Antiarthritic; Anti-HIV; Cytostatic; Muscular-Gen.; Immunosuppressive;

Antirheumatic.

MECHANISM OF ACTION - Androgen Receptor Modulator.

(I) was tested for antagonistic activity in a mammalian two-hybrid assay in CV-1 cells. The IC50 was found to be less than 1 micro M.

USE - (I) are used for modulating or activating a function mediated by the androgen receptor in at least one of bone and muscle tissue and blocked in the prostate or the uterus; for treating a condition (e.g. weakened muscle tone, osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia or other hematopoietic disorders, arthritic conditions, HIV-wasting, prostate cancer, cancer cachexia, muscular dystrophies, premature ovarian failure or autoimmune disease) caused by androgen deficiency or which can be ameliorated by androgen replacement, or which can be increased by androgen replacement; and for treating arthritic condition (e.g. rheumatoid arthritis or osteoarthritis) (all claimed).

ADVANTAGE - (I) increases the bone mineral density; reduces the risk of vertebral or non-vertebral fractures; and effects the bone turnover marker. (I) does not show any undesired side effects of non-tissue selective agonists of the androgen receptor.

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B01-A01; B01-A02; B01-C03; B01-C05; B03-G; B03-J; B04-H06; B04-J04B; B04-J05; B04-N04; B05-A01B; B05-B01E; B05-B01F; B05-B01G; B05-B02A3; B05-C07; B06-A01; B06-B01; B06-D01; B06-D18; B07-A02B; B07-D02; **B07-D03**; B07-D04C; B07-D12; B10-B03B; B10-C04A; B10-E04A; B14-C09; B14-D01A; B14-D02A; B14-E11; B14-E12; B14-F03; B14-F06; B14-F07; B14-G01B; B14-G02D; B14-J05; B14-N01; B14-N06B; B14-N07; B14-N14; B14-N17

TECH UPTX: 20040331

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: Preparation of (I) (where R1 is Me, and a-b is CF=CH) involves reacting 2-fluoro-4-methyl-3-oxo-4-aza-5alpha-androst-1-ene-17beta-carboxylic acid with R2R3NH in presence of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide HCl (EDC) and 1-hydroxy-7-azabenzotriazole (HOAt).

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Treatment: The treatment additionally comprises administering:

(1) an estrogen or its derivative, alone or in combination with a progestin or its derivative (preferably conjugated estrogen, equine estrogen, 17beta-estradiol, estrone, 17beta-ethynyl estradiol, 17beta-ethynyl estrodiol with at least one agent selected from norethindrone and medroxyprogesterone acetate);

(2) a bisphosphonate e.g. alendronate, clodronate, etidronate, ibandronate, incadronate, minodronate, neridronate, olpadronate, pamidronate, piridronate, risedronate, tiludronate, or zoledronate (preferably alendronate, especially alendronate monosodium trihydrate or alendronate monosodium monohydrate);

(3) an antiestrogen or a selective estrogen receptor modulator e.g. raloxifene, clomiphene, zuclomiphene, enclomiphene, nafoxidene, CI-680, CI-628, CN-55945-27, Mer-25, U-11555A, U-100A, tamoxifen, lasofoxifene, toremifene, azorxifene, EM-800, EM-652, TSE 424, droloxifene, idoxifene, or levormeloxifene;

(4) an alphavbeta3 integrin receptor antagonist;

(5) a cathepsin (preferably salmon calcitonin administered as a nasal spray) K inhibitor;

(6) an HMG-CoA reductase inhibitor e.g. lovastatin, simvastatin, dihydroxy-open acid simvastatin, pravastatin, fluvastatin, atorvastatin, cerivastatin, rosuvastatin, pitavastatin, or nisvastatin;
(7) an osteoclast vacuolar ATPase inhibitor;
(8) an antagonist of VEGF binding to osteoclast receptors;
(9) an activator of peroxisome proliferator-activated receptor gamma;
(10) calcitonin;
(11) a calcium receptor antagonist;
(12) parathyroid hormone (PTH) or its analog e.g. PTH subcutaneous injection, human PTH (1-84), human PTH (1-34), or other partial sequences, native or with substitutions;
(13) a **growth hormone secretagogue**;
(14) human **growth hormone**;
(15) insulin-like growth factor (IGF) e.g. IGF I and IGF II alone or in combination with IGF binding protein 3;
(16) a p38 protein kinase inhibitor;
(17) bone morphogenetic protein (BMP) e.g. BMP 2, BMP 3, BMP 5, BMP 6, BMP 7, TGFbeta, or GDF5;
(18) an inhibitor of BMP antagonism;
(19) a prostaglandin derivative e.g. agonists of prostaglandin receptors EP1, EP2, EP4, FP or IP;
(20) fibroblast growth factor (FGF) e.g. aFGF and bFGF;
(21) vitamin D or its derivative e.g. natural vitamin D, 25-OH-vitamin D3, 1alpha,25(OH)2 vitamin D3, 1alpha-OH-vitamin D3, 1alpha-OH-vitamin D2, dihydrotachysterol,26,27-F6-1alpha,25(OH)2 vitamin D3, 19-nor-1alpha,25(OH)2 vitamin D3, 22-oxacalcitriol, calcipotriol, 1alpha,25(OH)2-16-ene-23-yne-vitamin D3 (Ro 23-7553), EB1089, 20-epi-1alpha,25(OH)2 vitamin D3, KH1060, ED71, 1alpha,24(S)-(OH)2 vitamin D3, or 1alpha,24(R)-(OH)2 vitamin D3;
(22) vitamin K or its derivative;
(23) ipriflavone;
(24) fluoride salts e.g. sodium fluoride or monosodium fluorophosphate (MFP);
(25) dietary calcium supplement e.g. calcium carbonate, calcium citrate, or natural calcium salts; or
(26) osteoprotegerin.

ABEX UPTX: 20040331

SPECIFIC COMPOUNDS - 51 Compounds (I) are specifically claimed, e.g. N-(2-fluorophenylmethyl)-2-fluoro-4-methyl-3-oxo-4-aza-5alpha-androst-1-en-17beta-carboxamide (Ia).

ADMINISTRATION - The dosage is 0.01 - 1000 (preferably 0.1 - 20) mg/day, for oral administration. Other routes of administration include rectal, intravaginal, topical or parenteral (including subcutaneous, intramuscular or intravenous).

EXAMPLE - To a solution of 2-fluoro-4-methyl-3-oxo-4-aza-5alpha-androst-1-ene-17beta-carboxylic acid methyl ester (2.4 g) in 1,4-dioxane (50 mL) was added a solution of lithium hydroxide (0.41 g) in water (20 mL), and the mixture heated at 100 degrees C for 3 hours. After cooling, the mixture was worked up to give 2-fluoro-4-methyl-3-oxo-4-aza-5alpha-androst-1-ene-17beta-carboxylic acid (A) (2.2 g) as a pale yellow solid.
A mixture of (A) (0.12 g), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide HCl (EDC) (0.079 g), 1-hydroxy-7-azabenzotriazole (HOAt) (0.056 g), N-methyl morpholine (NMM) (0.15 mL) and 2-fluorobenzylamine (0.52 g) in N,N-dimethylformamide (DMF) (2 mL) was stirred for 4 hours. After work up N-(2-fluorophenylmethyl)-2-fluoro-4-methyl-3-oxo-4-aza-5alpha-androst-1-en-17beta-carboxamide (Ia) (0.12 g) was obtained as a pale yellow solid.

DEFINITIONS - Preferred Definitions:

R1 = methyl;
a-b = CF=CH or CHFCH2;
R2 = H;
R3 = (CH2)n-T, (CH2)n-cycloheteroalkyl; and
n = 0 or 1.

L115 ANSWER 22 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-457224 [43] WPIX
DOC. NO. CPI: C2003-121604
TITLE: Use of androstane 17-beta-carboxamides as modulators/activators of the androgen receptor for the treatment of e.g. osteoporosis and osteopenia in both men and women.
DERWENT CLASS: B01
INVENTOR(S): DUGGAN, M E; WANG, J; WHITMAN, D B
PATENT ASSIGNEE(S): (MERI) MERCK & CO INC; (DUGG-I) DUGGAN M E; (WANG-I) WANG J; (WHIT-I) WHITMAN D B
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2003029268	A1	20030410	(200343)*	EN	47	C07J003-00
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW						
EP 1434786	A1	20040707	(200444)	EN		C07J003-00
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR						
AU 2002331916	A1	20030414	(200461)			C07J003-00
US 2004220159	A1	20041104	(200473)			A61K031-58

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003029268	A1	WO 2002-US30864	20020927
EP 1434786	A1	EP 2002-768911	20020927
		WO 2002-US30864	20020927
AU 2002331916	A1	AU 2002-331916	20020927
US 2004220159	A1 Provisional	US 2001-327024P	20011003
		WO 2002-US30864	20020927
		US 2004-491403	20040330

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1434786	A1 Based on	WO 2003029268
AU 2002331916	A1 Based on	WO 2003029268

PRIORITY APPLN. INFO: US 2001-327024P 20011003; US 2004-491403 20040330
INT. PATENT CLASSIF.:
MAIN: A61K031-58; C07J003-00
SECONDARY: A61K031-56

BASIC ABSTRACT:

WO2003029268 A UPAB: 20040120

NOVELTY - Modulation or activation of a function mediated by the androgen receptor in a tissue involves administration of androstane 17- beta -carboxamides or its salt.

DETAILED DESCRIPTION - Modulation or activation (full or partial) of a function mediated by the androgen receptor in a tissue involves administration of androstane 17- beta -carboxamide of formula (I) or its salt.

a = single or double bond;

R1 = 1-3C alkyl, 3-6C cycloalkyl, phenyl, phenyl-1-3C alkyl (all optionally mono- to tri-substituted by halo, OH, amino, carboxy or 1-4C alkoxy);

R2 and R3 = 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 3-6C cycloalkyl, halo-1-4C alkyl, 1-6C alkylcarbonyl, 1-6C alkyloxycarbonyl, 1-6C alkylcarbonyloxy (all optionally mono- - tri-substituted by halo, OH, carboxy or 1-4C alkoxy), H, OH, 1-4C alkoxy, halo, carboxy or (1-6C)0-2 aminocarbonyloxy;

CR2+R3 = carbonyl, 1-6C alkylidene or spiro 3-6C cycloalkyl optionally substituted by 1-4C alkyl;

R2+R7 = fused cyclopropyl;

R4 and R7 = H or 1-4C alkyl;

R5 = H, 1-4C alkyl, 2-4C alkenyl or phenyl-1-3C alkyl; and

R6 = phenyl, naphthyl, benzimidazolyl, benzofuranyl, benzothiophenyl, benzoxazolyl, benzothiazolyl, benzodihydrofuranyl, indolyl, quinolyl, isoquinolyl, furanyl, thienyl, imidazolyl, oxazolyl, thiazolyl, isoxazolyl, isothiazolyl, pyrazolyl, pyrrolyl, pyridyl, pyrimidyl, pyrazinyl, thiadiazolyl, oxadiazolyl, triazolyl or tetrazolyl (all optionally mono- - tri-substituted by 1-8C alkyl, 3-8C cyclo(hetero)alkyl, phenyl, phenyl 1-3C alkyl, amino, amino-1-6C alkyl, 1-3C acylamino, 1-3C acylamino 1-6C alkyl, (di)1-6C alkylamino, (di)-1-6C alkylamino 1-6C alkyl, aminocarbonylamino, 1-4C alkoxy, 1-4C alkoxy 1-6C alkyl, 1-4C alkylthio, 1-4C alkylsulfinyl, 1-4C alkylsulfonyl, 1-4C alkylsulfonylamino, carboxy, carboxy-1-6C alkyl, 1-5C alkoxycarbonyl, 1-3C alkoxycarbonyl 1-6C alkyl, 1-5C alkylcarbonyloxy, OH, hydroxy-1-6C alkyl, CN, nitro, trifluoromethyl, trifluoromethoxy or trifluoroethoxy).

An INDEPENDENT CLAIM is also included for a composition comprising (I) and a bone-strengthening agent (II) selected from:

(1) an estrogen or its derivative, alone or in combination with a progestin or its derivative;

(2) a bisphosphonate;

(3) an antiestrogen or a selective estrogen receptor modulator;

(4) an alpha v beta 3 integrin receptor antagonist;

(5) a cathepsin K inhibitor;

(6) an HMG-CoA reductase inhibitor;

(7) an osteoclast vacuolar ATPase inhibitor;

(8) an antagonist of VEGF binding to osteoclast receptors;

(9) an activator of peroxisome proliferator-activated receptor gamma ;

(10) calcitonin;

(11) a calcium receptor antagonist;

(12) parathyroid hormone or its analog;

(13) a **growth hormone secretagogue**;

(14) human **growth hormone**;

(15) insulin-like growth factor;

(16) a P-38 protein kinase inhibitor;

(17) bone morphogenetic protein (BMP);

(18) an inhibitor of BMP antagonism;

(19) a prostaglandin derivative;

(20) vitamin D or its derivative;

(21) vitamin K or its derivative;
(22) ipriflavone;
(23) fluoride salts;
(24) dietary calcium supplement; or
(25) oxteoprotegerin.

ACTIVITY - Osteopathic; Antiinflammatory; Dermatological; Antiarteriosclerotic; Antilipemic; Antianemic; Cytostatic; Antiarthritic; Anti-HIV; Immunomodulator; Relaxant; Immunosuppressive; Gynecological.

MECHANISM OF ACTION - Selective androgen receptor modulator (SARM); Androgen receptor agonist and antagonist.

The compounds were tested for antagonistic activity using mammalian two-hybrid assay of N-terminus and C-terminus domains of the androgen receptor. The general formula (I) (no results for specific compounds are given) showed an IC50 value of less than 1 mu M.

USE - Compounds (I) are useful for activating a function mediated by the androgen receptor function blocked in the prostate of a male subject or in the uterus of a female subject and activated in bone and/or muscle tissue. (I) may also be used for treating a condition in a male or female subject caused by androgen deficiency, or which can be ameliorated by androgen replacement e.g. osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, female sexual dysfunction, post-menopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, aplastic anemia and other hematopoietic disorders, pancreatic cancer, renal cancer, prostate cancer, arthritis, joint repair, HIV-wasting, cancer, cachexia, muscular dystrophies, premature ovarian failure and autoimmune disease (all claimed).

ADVANTAGE - Compounds (I) produce positive responses of androgen replacement therapy without the undesired side effects and exert selective effects on different tissues of the body. (I) also have minimal negative effects on lipid metabolism. The compounds are also effective in raising blood cell numbers and, hence, can effectively treat hematopoietic disorders.

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B01-A01; B01-A02; B01-C04; B04-J04A; B04-N02A; B05-A01B; B05-B01G; B05-B02A3; B05-C07; B06-A01; B06-B01; B06-D01; B06-D02; B07-A02B; B07-D02; **B07-D03**; B07-D04C; B07-D05; B07-D12; B10-B02H; B10-E04D; B14-C09; B14-D01A; B14-D02A; B14-D02A2; B14-F03; B14-F06; B14-F07; B14-G02D; B14-H01; B14-J01A2; B14-J05A; B14-J05C; B14-N01; B14-N07A; B14-N13; B14-N14; B14-N16B; B14-N17; B14-P01

TECH UPTX: 20040120

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: (1) is conjugated estrogen, equine estrogen, 17beta-estradiol, estrone, 17beta-ethynyl estradiol, alone or in combination with an agent selected from norethindrone and medroxyprogesterone acetate.

(2) is (4-amino-1-hydroxybutylidene)-bisphosphonate, ((cycloheptylamino)-methylene)-bisphosphonate, (dichloromethylene)-bisphosphonate, (1-hydroxy-3-(1-pyrrolidinyl)-propylidene)-bisphosphonate, (1-hydroxyethylidene)-bisphosphonate, (1-hydroxy-3-(methylpentylamino)propylidene)-bisphosphonate, (6-amino-1-hydroxyhexylidene)-bisphosphonate, (3-(dimethylamino)-1-hydroxypropylidene)-bisphosphonate, (3-amino-1-hydroxypropylidene)-bisphosphonate, (2-(2-pyridinyl)ethylidene)-bisphosphonate, (1-hydroxy-2-(3-pyridinyl)-ethylidene)-bisphosphonate,

(((4-chlorophenyl)thio)methylene)-bisphosphonate, (1-hydroxy-2-(1H-imidazol-1-yl)ethylidene)-bisphosphonate or (1-hydroxy-2-imidazopyridin-(1,2-a)-3-ylethylidene)bisphosphonate.
(24) is calcium carbonate, calcium citrate or natural calcium salts.
Preferred Compound: (I) is preferably a compound of formula (III).
R2, R3 = H; or
R2+R3+C = methylene or a spirocyclopropy group;
R5, R7 = H or C; and
R6 = phenyl, napthyl or pyridyl (all optionally substituted by 1-3 of halo, 1-4C alkyl, amino, 1-3C acylamino, 1-4C alkylamino, di-(1-4C alkyl)amino, 1-4C alkoxy, 1-4C alkylthio, 1-4C alkysulfonyl, 1-4C alkylsulfonylamino, carboxy, 1-5C alkoxycarbonyl, 1-5C alkylcarbonyloxy, O, CN, nitro or trifluoromethyl).

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: (2) is raloxifene, clomiphene, zuclomiphene, enclomiphene, nafoxidene, CI-680, CI-628, CN-55,945-27, Mer-25, U-11,555A, U-100A, tamoxifen, lasofoxifene, toremifene, azorxifene, EM-800, EM-652, TSE 424, droloxifene, idoxifene or levormeloxifene.
(6) is lovastatin, simvastatin, dihydroxy-open acid simvastatin, pravastatin, fluvastatin, atorvastatin, cerivastatin, rosuvastatin, pitavastatin or nisvastatin.
(10) is salmon calcitonin administered as a nasal spray.
(17) is BMP 2, BMP 3, BMP 5, BMP 6, BMP 7, TGF beta or GDF5.
(15) is IGF I and IGF II alone or in combination with IGF binding protein 3.
(19) is agonist of prostaglandin receptors EP1, EP2, EP4, FP or IP. The fibroblast growth factor is aFGF or bFGF.
(12) is PTH subcutaneous injection, human PTH (1-84), human PTH (1-34) or other partial sequences, native or with substitutions.
(20) is natural vitamin D, 25-OH-vitamin D3, 1alpha,25(OH)2 vitamin D3, 1alpha-OH-vitamin D3, 1alpha-OH-vitamin D2, dihydrotachysterol, 26,27-F6-1alpha,25(OH)2 vitamin D3, 19-nor-1alpha,25(OH)2 vitamin D3, 22-oxacalcitriol, calcipotriol, 1alpha,25(OH)2-16-ene-23-yne-vitamin D3 (Ro 23-7553), EB1089, 20-epi-1alpha,25(OH)2 vitamin D3, KH1060, ED71, 1alpha,24(S)-(OH)2 vitamin D3 or 1alpha,24(R)-(OH)2 vitamin D3.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Component: (23) is sodium fluoride or monosodium fluorophosphate (MFP).
Preferred Method: The method further involves administering (II) and alendronate monosodium trihydrate.

ABEX UPTX: 20040120

WIDER DISCLOSURE - Compounds of formula (I) are disclosed as new.

SPECIFIC COMPOUNDS - 31 Compounds are specifically claimed as (I), e.g. 17beta-3-oxo-N-(2-trifluoromethylphenyl)-androst-4-en-17-carboxamide. 27 compounds as given in the specification e.g. (17beta)-3-oxo-N-(2-trifluoromethylphenyl)-androst-4-ene-17-carboxamide, (17beta)-3-oxo-N-(3-trifluoromethylphenyl)-androst-4-ene-17-carboxamide, (17beta)-3-oxo-N-(4-trifluoromethylphenyl)-androst-4-ene-17-carboxamide, (17beta)-N-(2-methoxyphenyl)-3-oxoandrost-4-ene-17-carboxamide and (17beta)-N-(3-methoxyphenyl)-3-oxoandrost-4-ene-17-carboxamide.

ADMINISTRATION - The daily dosage of (I) is 0.01-1000 (preferably 0.1-200) mg/day. The administration is oral, rectal, intravaginal, vaginally, as liposome, intranasally, intravenously, transdermally, topically or parenterally (including subcutaneously, intramuscularly or intravenously).

EXAMPLE - None given.

L115 ANSWER 23 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-599697 [64] WPIX
DOC. NO. CPI: C2002-169518
TITLE: Use of 8-(aminoalkoxyimino)-8H-dibenzo(a,e)triazolo(4,5-c)cycloheptene derivatives as a **growth hormone secretagogue** in the treatment or prevention of disease e.g. obesity, delayed wound healing.
DERWENT CLASS: B02
INVENTOR(S): BAGI, C M; DIXON, B R; RANGES, G; SCOTT, W J
PATENT ASSIGNEE(S): (FARB) BAYER CORP
COUNTRY COUNT: 98
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2002057241	A1	20020725	(200264)*	EN	53	C07D249-16
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW						
AU 2002243324	A1	20020730	(200427)			C07D249-16

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002057241	A1	WO 2001-US48259	20011214
AU 2002243324	A1	AU 2002-243324	20011214

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002243324	A1 Based on	WO 2002057241

PRIORITY APPLN. INFO: US 2000-258065P 20001222
INT. PATENT CLASSIF.:
MAIN: C07D249-16
SECONDARY: A61K031-4192; A61P019-00
BASIC ABSTRACT:
WO 200257241 A UPAB: 20021007
NOVELTY - A method of stimulating the release of **growth hormone** in a mammal involves administering 8-(aminoalkoxyimino)-8H-dibenzo(a,e)triazolo(4,5-c)cycloheptene derivatives.
DETAILED DESCRIPTION - A method of stimulating the release of **growth hormone** in a mammal involves administering a **growth hormone secretagogue** (A) of formula (I) or (II) or its salt.
T = -C=N-O-(CR1R2)n-NR3R4 or C(R14)-(CR1R2)n-NR3R4;
n = 2 - 4;
R1, R2 and R6 = H or 1-3C alkyl; or
R1+R2 = 3 - 7-membered ring;
R3 = H, 1-6C alkyl or C(=O)-R5-NH2;
R4 = H or 1-6C alkyl;
N(R3+R4) = 5 - 8-membered ring, which may contain an additional heteroatom selected from O or NR6;
R6 = H or 1-3C alkyl;

R5 = 1-6C alkyl;
R7 - R12 = H, halo, 1-3C alkyl, 1-3C alkoxy, NO2, CN or CF3;
R13 = 1-4C alkyl;
R14 = H or OH;

R1+R2 forms the ring can be on the same or adjacent carbon atom or carbon atoms that are 2 - 3 carbon atoms away from one another; and N(R3+R1) forms a 5 - 6-membered ring when n is 2 or 3.

An INDEPENDENT CLAIM is included for treatment or prevention of a disease or condition characterized by low bone mass, involving administering (A).

ACTIVITY - Vulnerary; Cardiant; Anorectic; Osteopathic; Dermatological; Nootropic; Antiinflammatory.

MECHANISM OF ACTION - Stimulator of release of **growth hormone**; Bone growth promoter; Promoter of healing of a bone fracture.

The compound of formula (I) in which (T is -C=N-O-(CR1R2)n-NR3R4) tested for stimulation of the **growth hormone** release from rat pituitary cells. The release of **growth hormone** (ng/ml) by (I) was (10 nM) was around 160, control was around 80 and GHRP6 was above 160. No results for specific compounds are given.

USE - As a **growth hormone secretagogue** for treating or preventing a disease or condition resulting from a deficiency of **growth hormone** in a mammal e.g. delayed wound healing; skin burns; decreased muscle mass; congestive heart failure; growth retardation resulting from renal failure or renal insufficiency, chronic illness, obesity, Prader-Willi syndrome, Turner's syndrome, Down's syndrome, Noonan's syndrome; immune deficiencies; physiological short stature; intrauterine growth retardation; and hyperinsulinemia. For treating or preventing a disease or condition that is treatable by increasing levels of **growth hormone** in a mammal and which causes low bone mass e.g. osteoporosis, osteopenia, osteotomy, childhood idiopathic bone loss, bone loss associated with periodontitis and bone metastases (all claimed).

ADVANTAGE - (A) promotes or enhances bone growth selected from periosteal bone growth, endocortical bone growth and cancellous bone growth and healing of a bone fracture in a mammal. (A) increases endogenous levels of **growth hormone.**

Dwg.0/1

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B01-B03; B01-C06; B04-A06; B04-C01A; B04-C01B; B04-H03; B04-H06; B04-H06H; B04-J02; B04-J04B; B04-N02; B05-A01B; B05-B01E; B05-B01F; B05-B01G; B05-C07; B06-A01; B06-B01; B06-D01; B06-D16; B06-D18; **B07-D03**; B07-D04A; B07-D09; B10-B03B; B10-E02; B14-F01B; B14-F09; B14-J05; B14-L01; B14-N01; B14-N17A; B14-N17B

TECH UPTX: 20021007

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: The method further involves administering a bone anti-resorptive agent, a bone anabolic agent or a second **growth hormone secretagogue** in combination with (A).

Preferred Components: The bone anti-resorptive agent is droloxifene, raloxifene, tamoxifen, 4-hydroxy-tamoxifen, toremifene, centchroman, clometherone, delmadinone, levormeloxifene, idoxifene, nafoxidine, nitromifene, ormeloxifene, trioxifene, tiludronic acid, zoledronic acid, alendronic acid, ibandronic acid, risedronic acid, etidronic acid, clodronic acid, pamidronic acid, dimethyl-APD, YM-175 or BM-210995.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Agent: The bone anabolic agent is

bone morphogenic proteins, thyrotropin releasing hormone or their active fragment; diethylstilbeserol, estrogens, beta-agonists, parathyroid hormone or their active fragments; theophylline, anabolic steroids, enkephalins, prostaglandins and their agonists/antagonists; or sodium fluoride. The second **growth hormone secretagogue** is hexarelin, GHRP-6, GHRP-1, GHRP-2, GHRF or their analogs, IGF-1, IGF-2, B-HT920, clondine, sumitriptan, physostigmine or pyridostigmine.

ABEX UPTX: 20021007

SPECIFIC COMPOUNDS - The use of 20 Compounds are specifically claimed as (A) e.g. 1-Phenyl-1H-1,2,3-triaza-dibenzo(e,h)azulen-8-one O-(1-(2-(1-amino-cyclopropyl)-acetyl)-piperidin-4-yl)-oxime of formula (Ia).

ADMINISTRATION - (A) may be administered orally in a dosage of 0.01 - 200 mg/kg, dermally, parenterally, by injection (including intravenous, intramuscular, subcutaneous, or parenteral injection) in a dosage of 0.01 - 200 mg/kg, by inhalation in a dosage of 0.01 - 10 mg/kg or spray, or sublingually, rectally in a dosage of 0.01 - 200 mg/kg, or vaginally in a dosage of 0.01 - 200 mg/kg, topically in a dosage of 0.01 - 200 mg/kg and transdermally in a dosage of 0.01 - 200 mg/kg.

EXAMPLE - No relevant example given.

DEFINITIONS - Preferred Definitions:
R1, R2 = H or 1-3C alkyl;
R3 = C(=O)-R5-NH2; and
NR3+R5 = 5 - 6-membered ring.

L115 ANSWER 24 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-636510 [68] WPIX
DOC. NO. CPI: C2004-013547
TITLE: Use of 2-substituted dibenzo(a,e)1,2,3-triazolo(4,5-c)(7)annulen-8-ones as **growth hormone secretagogues** for treating e.g. osteoporosis.
DERWENT CLASS: B02 B05
INVENTOR(S): BAGI, C M; DIXON, B R; RANGES, G; SCOTT, W J
PATENT ASSIGNEE(S): (FARB) BAYER CORP
COUNTRY COUNT: 98
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2002056873	A2	20020725	(200268)*	EN	34	A61K031-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW						
AU 2002245118	A1	20020730	(200427)			A61K031-00

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002056873	A2	WO 2001-US48258	20011214
AU 2002245118	A1	AU 2002-245118	20011214

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002245118	A1 Based on	WO 2002056873

PRIORITY APPLN. INFO: US 2000-258064P 20001222
INT. PATENT CLASSIF.:
MAIN: A61K031-00
SECONDARY: A61K031-4192; A61K031-454; A61K045-06; A61P003-04; A61P003-10; A61P009-04; A61P017-02; A61P019-08; A61P021-06; A61P037-00

BASIC ABSTRACT:

WO 200256873 A UPAB: 20040429

NOVELTY - Treatment or prevention of a disease or condition resulting from a deficiency of **growth hormone** in a mammal involves administering **growth hormone secretagogue** (I).

DETAILED DESCRIPTION - Treatment or prevention of a disease or condition resulting from a deficiency of **growth hormone** in a mammal involves administering **growth hormone secretagogue** of formula (I) or its salt.

n = 2-4;

R1, R2 = H or 1-3C alkyl;

R1+R2 = 3-7 membered ring;

R3 = H, 1-6C alkyl or C(=O)-R5-NH2;

NR1R3 = 5-6 membered ring;

R4 = H or 1-6C alkyl;

NR3R4 = 5-8 membered ring (optionally containing O or NR6);

R5 = 1-6C alkyl;

R6 = H or 1-3C alkyl; and

R7-R10 = H, halo, 1-3C alkyl, 1-3C alkoxy, NO2, CN or CF3;

provided that R1+R2 can be on the same carbon atom, adjacent carbon atoms or carbon atoms that are 2-3 atoms away from one another. When n = 2 or 3, R1 and R3 join together with N to form a 5-6 membered ring.

ACTIVITY - Cardiant; Anabolic; Anorectic; Immunoprotective; Osteopathic; Vulnerary; Antidiabetic.

An OVX rat model was administered with fluorochrome bone markers for histomorphometric measurements before starting treatment. All rats were administered orally with vehicle or 2-(2-dimethylamino-ethyl)-2H-1,2,3-triaza-dibenzo(e,h)azulen-8-one (20 mg/kg) during a 5 week period. Changes in the bone mineral area at femoral midshaft in ovariectomized rats were observed. No specific results were given.

MECHANISM OF ACTION - None given.

USE - For treating or preventing a disease or condition resulting from a deficiency of **growth hormone** e.g. delayed wound healing, skin burns, decreased muscle mass, congestive heart failure, growth retardation, obesity, immune deficiency, physiological short stature, intrauterine growth retardation, hyperinsulinemia, osteoporosis, osteopenia, osteotomy, childhood idiopathic bone loss, bone loss associated with peridontitis, bone metastases (the growth retardation results from renal failure or renal insufficiency, chronic illness, obesity, Prader-Willi syndrome, Turner's syndrome, Down's syndrome, Noonan's syndrome) (all claimed). Also for stimulating the immune system in companion animals, treating disorders of aging in companion animals, promoting growth in livestock and stimulating wool growth in sheep.

ADVANTAGE - (I) Increases levels of **growth hormone** in a mammal, enhances bone growth selected from periosteal bone growth, endocortical bone growth or cancellous bone growth, increases endogenous levels of **growth hormone** and enhances bone fracture healing.

Dwg.0/4
FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B01-A01; B01-B03; B01-C04; B04-A06; B04-C01A; B04-C01B; B04-H03; B04-N04A; B05-B01E; B05-B01F; B05-B01G; B05-C07; B06-A01; B06-B01; B06-D01; B06-D16; **B07-D03**; B07-D04A; B07-D09; B10-B03B; B14-E12; B14-F01; B14-G01; B14-N01; B14-N17A; B14-N17B; B14-S04; B14-S12

TECH UPTX: 20040429

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: The process involves administering bone anti-resorptive agent, bone anabolic agent or a second **growth hormone secretagogue.**

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The bone anti-resorptive agent is droloxifene, raloxifene, tamoxifen, 4-hydroxy-tamoxifen, toremifene, centchroman, clometherone, delmadinone, levormeloxifene, idoxifene, nafoxidine, nitromifene, ormeloxifene, trioxifene, tiludronic acid, zoledronic acid, alendronic acid, ibandronic acid, risedronic acid, etidronic acid, clodronic acid, pamidronic acid, dimethyl-APD, YM-175 (RTM) and BM-210995 (RTM). The bone anabolic agent is bone morphogenic proteins, thyrotropin releasing hormone, diethylstilbeserol, estrogens, beta-agonists, parathyroid hormone, theophylline, anabolic steroids, enkephalins, prostaglandins, and sodium fluoride. The second **growth hormone secretagogue** is selected from hexarelin, GHRP-6, GHRP-1, GHRP-2, GHRF-6, IGF-1, IGF-2, B-HT920, clondine, sumitriptan, physostigmine and pyridostigmine.

ABEX UPTX: 20040429

SPECIFIC COMPOUNDS - 7 Compounds (I) are specifically claimed e.g. 2-(2-dimethylamino-ethyl)-2H-1,2,3-triaza-dibenzo(e,h)azulen-8-one (Ia).

ADMINISTRATION - Administration of (I) is 0.01-200 mg/kg orally, dermally, parenterally, by inhalation spray, sublingually, rectally, vaginally, or by injection (including intravenous, intraarticular, intramuscular, subcutaneous, or by infusion).

L115 ANSWER 25 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-098049 [13] WPIX
DOC. NO. CPI: C2002-030599
TITLE: New pyridine containing compounds useful as 3-Hydroxy-3-methylglutaryl-coenzyme A reductase inhibitor in the treatment of e.g. cholesterol-related diseases.
DERWENT CLASS: B02
INVENTOR(S): CHEN, B; ROBL, J A; SUN, C; ROBI, J A
PATENT ASSIGNEE(S): (CHEN-I) CHEN B; (ROBL-I) ROBL J A; (SUNC-I) SUN C; (BRIM) BRISTOL-MYERS SQUIBB CO
COUNTRY COUNT: 97
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2001096347	A1	20011220	(200213)*	EN	106	C07D491-04
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW						
US 2002013334	A1	20020131	(200216)			A61K031-4741

AU 2001066858	A	20011224	(200227)			C07D495-04
US 2002094977	A1	20020718	(200254)			C07D498-02
NO 2002006012	A	20030203	(200322)			C07D491-04
EP 1294728	A1	20030326	(200323)	EN		C07D495-04
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR						
CZ 2002003930	A3	20030312	(200324)			C07D491-04
KR 2003036225	A	20030509	(200358)			C07D491-044
US 6627636	B2	20030930	(200367)			A61K031-4353
CN 1436192	A	20030813	(200373)			C07D491-04
JP 2004503557	W	20040205	(200412)		177	C07D471-04
HU 2003002937	A2	20031229	(200413)			C07D495-04
MX 2002012252	A1	20030601	(200417)			A61K031-55
US 2004092573	A1	20040513	(200432)			A61K031-40
ZA 2002010103	A	20040526	(200438)		111	C07D000-00
US 6812345	B2	20041102	(200472)			C07D491-044
NZ 523627	A	20041029	(200474)			C07D495-04
BR 2001011599	A	20041013	(200477)			C07D495-04

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2001096347	A1		WO 2001-US18864	20010612
US 2002013334	A1	Provisional	US 2000-211595P	20000615
			US 2001-875155	20010606
AU 2001066858	A		AU 2001-66858	20010612
US 2002094977	A1	Provisional	US 2000-211595P	20000615
		CIP of	US 2001-875155	20010606
			US 2001-7407	20011204
NO 2002006012	A		WO 2001-US18864	20010612
			NO 2002-6012	20021213
EP 1294728	A1		EP 2001-944447	20010612
			WO 2001-US18864	20010612
CZ 2002003930	A3		WO 2001-US18864	20010612
			CZ 2002-3930	20010612
KR 2003036225	A		KR 2002-717086	20021214
US 6627636	B2	Provisional	US 2000-211595P	20000615
		CIP of	US 2001-875155	20010606
			US 2001-7407	20011204
CN 1436192	A		CN 2001-811211	20010612
JP 2004503557	W		WO 2001-US18864	20010612
			JP 2002-510488	20010612
HU 2003002937	A2		WO 2001-US18864	20010612
			HU 2003-2937	20010612
MX 2002012252	A1		WO 2001-US18864	20010612
			MX 2002-12252	20021211
US 2004092573	A1	Provisional	US 2000-211595P	20000615
		CIP of	US 2001-875155	20010606
			US 2003-602752	20030624
ZA 2002010103	A		ZA 2002-10103	20021212
US 6812345	B2	Provisional	US 2000-211595P	20000615
		CIP of	US 2001-875155	20010606
		Div ex	US 2001-7407	20011204
			US 2003-602752	20030624
NZ 523627	A		NZ 2001-523627	20010612
			WO 2001-US18864	20010612
BR 2001011599	A		BR 2001-11599	20010612
			WO 2001-US18864	20010612

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001066858	A Based on	WO 2001096347
EP 1294728	A1 Based on	WO 2001096347
CZ 2002003930	A3 Based on	WO 2001096347
JP 2004503557	W Based on	WO 2001096347
HU 2003002937	A2 Based on	WO 2001096347
MX 2002012252	A1 Based on	WO 2001096347
US 6812345	B2 Div ex	US 6627636
NZ 523627	A Based on	WO 2001096347
BR 2001011599	A Based on	WO 2001096347

PRIORITY APPLN. INFO: US 2000-211595P 20000615; US
2001-875155 20010606; US
2001-7407 20011204; US
2003-602752 20030624

INT. PATENT CLASSIF.:
MAIN: A61K031-40; A61K031-4353; A61K031-4741; A61K031-55; C07D000-00; C07D491-044; C07D498-02
SECONDARY: A61K031-4365; A61K031-4743; A61K031-4745; A61K045-06; A61P001-04; A61P001-16; A61P003-00; A61P003-04; A61P003-06; A61P003-10; A61P007-02; A61P009-00; A61P009-10; A61P013-12; A61P015-08; A61P015-10; A61P017-00; A61P019-00; A61P019-10; A61P025-28; A61P031-18; A61P035-00; A61P043-00; C07D491-02; C07F009-28
ADDITIONAL: C07D221-00; C07D223-00; C07D313-00; C07D337-00; C07D471-04; C07D491-04; C07D495-04
INDEX: C07D221:00; C07D491-04

BASIC ABSTRACT:

WO 200196347 A UPAB: 20020226

NOVELTY - Pyridine-containing compounds (I) are new.

DETAILED DESCRIPTION - Pyridine-containing compounds of formula (I), their salts (where R3 is H), ester, prodrug ester and stereosisomer are new.

X = O, S, or NR7;

Z' = -CH(OH)-CH2-C(R8)(OH)-CH2-CO2R3 or a group of formula (i);

asterisk = attachment point;

n = 0 or 1;

R1 and R2 = alkyl, aryalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl or cycloheteroalkyl;

R3 and R8 = H or lower alkyl;

R4 = H, halo, CF3, hydroxy, alkyl, alkoxy, alkanoylamino, aroylamino, or cyano;

R7 = H, alkyl, aryl, alkanoyl, aroyl, or alkoxycarbonyl;

R9 and R10 = H or alkyl;

R9+R10 = 3 - 7 membered carbocyclic ring;

dashed line = cis or trans single or double bond.

INDEPENDENT CLAIMS are also included for the following:

(1) a pharmaceutical combination comprising (I) and at least one hypolipidemic agent (1), lipid-lowering agent (2), lipid agent (3), lipid modulating agent (4), at least one other type of therapeutic agent (5) including antidiabetic agent (6), anti-obesity agent (7), antihypertensive agent (8), platelet aggregation inhibitor (9), anti-dementia agent (10), anti-Alzheimer's agent (11), antiosteoporosis agent (12), and/or hormone replacement therapeutic agent (13), other cardiovascular agent (14) including anti-anginal agent (15), anti-arrhythmic agent (16), anti-atherosclerosis agent (17), anti-inflammatory agent (18),

anti-arthritis agent (19), anti-platelet agent (20), anti-heart failure agent (21)), anti-cancer agent (22), anti-infective agent (23), hormone replacement agent (24), **growth hormone secretagogues** (25), selective androgen receptor modulator (26), and/or immunomodulatory agent (27); and

(2) an intermediate of formula (II).

Q = -CO2T, CH2OH, -CH2-halide, -CH2-P(=O)(W)-W or a group of formula (ii);

T = alkyl; and

W = aryl, alkyl or alkoxy.

ACTIVITY - Antilipemic; Antiarteriosclerotic; Nootropic; Neuroprotective; Osteopathic; Cerebroprotective; Cardiant; Antiangial; Hypotensive; Antidiabetic; Anorectic; Cytostatic; Antiinflammatory; Litholytic; Hepatotropic; Anti-HIV; Antipsoriatic; Antiarrhythmic; Vasotropic; Anorectic.

MECHANISM OF ACTION - 3-Hydroxy-3-methylglutaryl-coenzyme A reductase (HMG-CoA reductase) inhibitor.

USE - (I) are used for inhibiting cholesterol biosynthesis or lowering blood serum cholesterol levels and/or modulating blood serum cholesterol levels, lowering low density lipoprotein (LDL) cholesterol and/or increasing high density lipoprotein (HDL) cholesterol, or treating dyslipidemia, mixed dyslipidemia, LDL Pattern B, LDL Pattern A, hyperlipidemia, hypercholesterolemia, hypo alpha -lipoproteinemia, hyperlipoproteinemia or hypertriglyceridemia, and other aberrations of apolipoprotein B metabolism, reducing levels of Lp(a); treating or preventing other cholesterol-related diseases; treating, preventing or reversing progression of atherosclerosis, Alzheimer's disease, osteoporosis, osteopenia; reducing inflammatory markers, reducing C-reactive protein, or preventing or treating low grade vascular inflammation, stroke, dementia, coronary heart disease, primary and secondary prevention of myocardial infarction, stable and unstable angina, primary prevention of coronary events, secondary prevention of cardiovascular events, peripheral vascular disease, peripheral arterial disease, acute vascular syndromes, reducing the risk of undergoing myocardial revascularization procedure, microvascular diseases such as nephropathy, neuropathy, retinopathy and nephrotic syndrome, hypertension, Type I and 2 diabetes and related diseases, insulin resistance, hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol, obesity, Syndrome X, diabetic complications, dysmetabolic syndrome, and related diseases, and sexual dysfunction, malignant lesions, premalignant lesions, gastrointestinal malignancies, liposarcomas and epithelial tumors, cancer induced asthenia (fatigue), irritable bowel syndrome, Crohn's disease, gastric ulceritis, and gall stones, and HIV infection, drug-induced lipodystrophy, proliferative diseases such as psoriasis, improving coagulation homeostasis, reducing PAI-1 activity, reducing fibrinogen, and/or reducing platelet aggregation, and/or improving endothelial function, cerebrovascular diseases (all claimed).

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B01-C06; B01-D02; B04-C03; B04-J03A; B04-N02; B04-N04; B05-B01E; B06-A02; B06-D02; B06-D04; B06-D07; B06-D09; B06-D13; B06-D16; B06-D18; B06-F03; B07-A02; B07-A02B; B07-A03; B07-D02; **B07-D03**; B07-D04C; B07-D05; B07-D06; B07-D12; B07-D13; B07-E01; B07-E04; B07-F01; B08-C01; B10-A08; B10-A13D; B10-A15; B10-A17; B10-B03B; B10-B04B; B10-C03; B10-C04B; B14-C03; B14-C09; B14-D02; B14-D03; B14-D06; B14-D07C; B14-E10; B14-F01; B14-F02; B14-F02B; B14-F06;

B14-F07; B14-H01; B14-J01A4; B14-J04; B14-L06;
B14-N01; B14-N03; B14-N11; B14-S04

TECH UPTX: 20020226

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: The saturated derivative of (IB) (where a is CH2-CH2) is obtained by catalytic (Pd/C, Pt/C, Pd(OH)2) hydrogenation of (IA).

Preferred Compound: The compound is of formula (III) or its internal lactone, (IV), its alkali or alkaline earth metal salt, amino acid salt, or acid addition salt via the pyridine of the corresponding delta lactone, (V) or (VI) or their salts or internal lactones.

R'3 = H, an alkali or alkaline earth metal ion, an amino acid;
R5 and R6 = H, halo or alkyl;
R'2 = alkyl or cycloalkyl;
W' = -CH(CH3)2 or cyclopropyl.

The intermediate is of formula (VIII) - (XI).

G' = CO2R, -CH2-OH, -CH2-halide, or -CH2-P(W)2=O; and
dashed line = single or double bond.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: (1) - (4) or (17) comprises at least one metalloprotease (MTP) inhibitor, 3-huydroxy-3-methylglutaryl-coenzyme-A (HMG CoA) reductase inhibitor, squalene synthetase inhibitor, fibric acid derivative, peroxisome proliferator activated receptors (PPAR)alpha agonist, PPAR dual alpha/gamma agonist, PPAR delta agonist, acyl coenzyme A;cholesterol acyl transferase (ACAT) inhibitor, lipoxygenase inhibitor, cholesterol absorption inhibitor, ileal Na+/bile acid cotransporter inhibitor, upregulator of low density lipoprotein (LDL) receptor activity, cholesteryl ester transfer protein inhibitor, bile acid sequestrant, or nicotinic acid and their derivatives, adenosine triphosphatase (ATP) citrate lyase inhibitor, phytoestrogen compound, an high density lipoprotein (HDL) upregulator, LDL catabolism promoter, antioxidant, phosphpolylipase (PLA)-2 inhibitor, antihomocysteine agent, HMG-CoA synthase inhibitor, lanosterol demethylase inhibitor, or sterol regulating element binding protein-I agent. (6) is at least one antidiabetic agent or antihyperglycemic agent including insulin **secretagogues** or insulin sensitizer, which may include biguanide, sulfonyl urea, PTP (undefined)-1B inhibitor, aldose reductase inhibitor, glucosidase inhibitor, PPARgamma agonist, PPARalpha agonist, PPARdelta antagonist or agonist, aP2 inhibitor, PPAR alpha/gamma dual agonist, dipeptidyl peptidase IV (DP4) inhibitor, SGLT2 inhibitor, glycogen phosphorylase inhibitor, and/or meglitinides, insulin, and/or glucagon-like peptide-1 (GLP-1) or their mimetics (preferably metformin, glyburide, glimepiride, glipyride, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, troglitazone, rosiglitazone, insulin, Gl-262570, isaglitazone, JTT-501, NN-2344, L895645, YM-440, R-119702, AJ9677, repaglinide, nateglinide, KAD1129, AR-HO39242, GW-409544, KRP297, AC2993, LY315902, P32/98 and/or NVP-DPP-728A). (5) is a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin (and dopamine) reuptake inhibitor, an aP2 inhibitor, a thyroid receptor beta drug, an anorectic agent, a PTP-1B inhibitor, a CCKA agonist, a neuropeptide Y antagonist, a melanocortin-4-receptor agonist, a PPAR modulator which is a PPARgamma antagonist, PPARalpha agonist, and/or PPARdelta antagonist, a leptin inhibitor such as a leptin receptor activator, a fatty acid oxidation upregulator or inducer. (4) is an MTP inhibitor, an HMG CoA reductase inhibitor, a squalene synthetase inhibitor, a fibric acid derivative, an upregulator of LDL receptor activity, a lipoxygenase inhibitor, or an ACAT inhibitor (preferably pravastatin, lovastatin, simvastatin, atorvastatin, cerivastatin, fluvastatin, pitavastatin, rosuvastatin, fenofibrate, gemfibrozil, clofibrate, avasimibe, TS-962, MD-700, cholestagel, niacin, and/or LY295427). (3) is a cholesteryl ester transfer protein inhibitor. (8) is an ACE inhibitor (preferably captopril, fosinopril, enalapril,

lisinopril, quinapril, benazepril, fentiapril, ramipril or moexipril, especially ramipril), angiotensin II receptor antagonist (preferably irbesartan, losartan or valsartan), NEP (undefined) inhibitor, a NEP/ACE inhibitor (preferably omapatrilat, gemopatrilat, or CGS 30440, especially omapatrilat or gemopatrilat), a calcium channel blocker, a T-channel calcium antagonist, a a-adrenergic blocker, a diuretic, a a-adrenergic blocker, a dual action receptor antagonist, or a heart failure drug (preferably amlodipine besylate, prazosin HCI, verapamil, nifedipine, nadolol, propranolol, or clonidine HCI, carvediol, atenolol, hydrochlorothiazide, torasemide, furosemide, spironolactone or indapamide). (7) is orlistat, ATL962, AJ9677, L750355, CP331648, sibutramine, topiramate, axokine, dexamphetamine, phentermine, phenylpropanolamine, and/or mazindol, P57 or CP-644673. (9) is aspirin, clopidogrel, ticlopidine, dipyridamole, ifetroban, abciximab, tirofiban, eptifibatide, or anagrelide (preferably aspirin and/or clopidogrel). (5) is (10) or (11) (preferably Cognex (RTM; tacrine HCl), Aricept (RTM; donepezil), gamma secretase inhibtor, a beta-secretase inhibitor and/or antihypertensive agent), (12) (preferably parathyroid hormone, a bisphosphonate, alendronate, a Ca receptor agonist or a progestin receptor agonist), (13) (preferably a selective estrogen receptor modulator), a tyrosine kinase inhibitor, a selective androgen receptor modulator, (16) (preferably a beta-blocker, or a calcium channel blocker, or an a-adrenergic blocker), coenzyme Q sub. 10, an agent that upregulates type III endothelial cell nitric acid syntase, a chondroprotective compound (preferably polysulfated glycosaminoglycan, glucosamine, chondroitin sulfate, hyaluronic acid, pentosan polysulfate, doxycycline or minocycline), a cyclooxygenase (COX)-2 inhibitor (preferably Celebrex or Vioxx or a glycoprotein IIa/IIIb receptor antagonist), a 5-HT reuptake inhibitor, (25), (17), (23), an immunosuppressant for use in transplantation, or an antineoplastic agent.

ABEX UPTX: 20020226

WIDER DISCLOSURE - The disclosure states (II) are new.

SPECIFIC COMPOUNDS - 30 Compounds (I) are disclosed e.g. 7-(2-cyclopropyl-4-(4-fluorophenyl)-5,6-dihydro-7-oxa-1-aza-dibenzo(a,c)cyclohepten-3-yl)-3,5-dihydroxy-hept-6-enoic acid sodium salt of formula (Ia).

ADMINISTRATION - The compounds are administered orally or parenterally in a dosage of 0.1-500 (preferably 0.2 - 100) mg 1-4 times per day.

EXAMPLE - A solution of (2-cyclopropyl-4-(4-fluorophenyl)-5,6-dihydro-7-oxa-1-aza-dibenzo(a,c)cyclohepten-3-ylmethyl)-phosphonic acid diethyl ester (I) (2.29 g) in dry tetrahydrofuran (THF) (20 ml) was cooled to -78degreesC, treated with 2.37M n-butyl lithium (2.41 ml) and stirred for 40 minutes. The solution was treated via cannula with -78degreesC solution of 6-formyl-2,2-dimethyl-(1,3)dioxan-4--yl)-acetic acid tert-butyl ester (2.36 g) in dry tetrahydrofuran (THF) (10 ml). The reaction mixture was stirred for 1 hour at -78degreesC, for 1 hour at -10degreesC and for 5 hours at room temperature, quenched with 25% ammonium chloride solution (12 ml) and then extracted. Then the combined organic extracts were washed, filtered, evaporated and dried. The crude product was chromatographed to give (6-(2-(2-cyclopropyl-4-(4-fluorophenyl)-5,6-dihydro-7-oxa-1-aza-dibenzo(a,c)cyclohepten-3-yl)-vinyl)-2,2-dimethyl-(1,3)dioxan-4-yl)-acetic acid tert-butyl ester (II) (878 mg). A solution of (II) (850 mg) in dry dichloromethane (20 ml) was cooled to 0degreesC, treated with trifluoroacetic acid (1.85 ml), stirred at 0degreesC for 5 minute, and then at room temperature for 4.5 hours. The reaction mixture was poured slowly into a flask containing ethyl acetate (300 ml), saturated sodium bicarbonate (40 ml), and rinsed. The mixture was stirred

well and the phases separated. The organic phase was washed, filtered, evaporated, dried and chromatographed to give (6-(2-(2-cyclopropyl-4-(4-fluorophenyl)-5,6-dihydro-7-oxa-1-aza-dibenzo(a,c)cyclohepten-3-yl)-4-hydroxy-tetrahydro-pyran-2-one (III) (570 mg). A solution of (III) (550 mg) in dry THF (10 ml) was treated with 1N sodium hydroxide (1.46 ml) and stirred at room temperature for 10 minutes. The reaction mixture was evaporated to dryness and the residual solid was dissolved in a mixture of water (8.7 ml) and 1N sodium hydroxide (70 ml). The solution was eluted on an SP 207 column (Na+ form). The desired fractions were combined and evaporated to dryness. The semi-solid obtained was dissolved in water (300 ml) and lyophilized to give 7-(2-cyclopropyl-4-(4-fluorophenyl)-5,6-dihydro-7-oxa-1-aza-dibenzo(a,c)cyclohepten-3-yl)-3,5-dihydroxy-hept-6-enoic acid sodium salt (583 mg).

DEFINITIONS - Preferred Definitions:
dashed line = trans double bond;
R1 = 4-fluorophenyl, 4-fluoro-3-methylphenyl, 3,5-dimethylphenyl;
R2 = isopropyl, tert-butyl or cyclopropyl;
R4 = H;
n = zero;
X = O.

L115 ANSWER 26 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-098045 [13] WPIX
DOC. NO. CPI: C2002-030595
TITLE: New pyridine-containing compound for treating e.g. hyperlipedemia, hypercholesterolemia, Alzheimer's disease, osteoporosis.
DERWENT CLASS: B05
INVENTOR(S): CHEN, B; ROBL, J A; SUN, C
PATENT ASSIGNEE(S): (CHEN-I) CHEN B; (ROBL-I) ROBL J A; (SUNC-I) SUN C; (BRIM) BRISTOL-MYERS SQUIBB CO
COUNTRY COUNT: 97
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2001096311	A2	20011220	(200213)*	EN	106	C07D221-06
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW						
US 2002028826	A1	20020307	(200221)			C07D221-06
AU 2001066860	A	20011224	(200227)			
US 2002061901	A1	20020523	(200239)			A61K031-4747
NO 2002006011	A	20030212	(200321)			C07D221-06
EP 1294696	A2	20030326	(200323)	EN		C07D221-06
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR						
CZ 2002003931	A3	20030312	(200324)			C07D221-06
KR 2003010720	A	20030205	(200338)			C07D405-06
BR 2001011571	A	20030701	(200356)			C07D221-06
US 6620821	B2	20030916	(200362)			A61K031-435
CN 1436174	A	20030813	(200373)			C07D221-06
US 2004024216	A1	20040205	(200411)			C07D405-02
JP 2004503541	W	20040205	(200412)		183	C07D221-16
HU 2003002955	A2	20031229	(200413)			C07D221-06
MX 2002012415	A1	20030601	(200417)			C07D221-06

ZA 2002010102 A 20040526 (200438) 120 C07D000-00

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001096311	A2	WO 2001-US18868	20010612
US 2002028826	A1 Provisional	US 2000-211594P	20000615
		US 2001-875218	20010606
AU 2001066860	A	AU 2001-66860	20010612
US 2002061901	A1 Provisional	US 2000-211594P	20000615
	CIP of	US 2001-875218	20010606
		US 2001-8154	20011204
NO 2002006011	A	WO 2001-US18868	20010612
		NO 2002-6011	20021213
EP 1294696	A2	EP 2001-944449	20010612
		WO 2001-US18868	20010612
CZ 2002003931	A3	WO 2001-US18868	20010612
		CZ 2002-3931	20010612
KR 2003010720	A	KR 2002-717087	20021214
BR 2001011571	A	BR 2001-11571	20010612
		WO 2001-US18868	20010612
US 6620821	B2 Provisional	US 2000-211594P	20000615
	CIP of	US 2001-875218	20010606
		US 2001-8154	20011204
CN 1436174	A	CN 2001-811219	20010612
US 2004024216	A1 Provisional	US 2000-211594P	20000615
	CIP of	US 2001-875218	20010606
	Div ex	US 2001-8154	20011204
		US 2003-602753	20030624
JP 2004503541	W	WO 2001-US18868	20010612
		JP 2002-510454	20010612
HU 2003002955	A2	WO 2001-US18868	20010612
		HU 2003-2955	20010612
MX 2002012415	A1	WO 2001-US18868	20010612
		MX 2002-12415	20021213
ZA 2002010102	A	ZA 2002-10102	20021212

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001066860	A Based on	WO 2001096311
EP 1294696	A2 Based on	WO 2001096311
CZ 2002003931	A3 Based on	WO 2001096311
BR 2001011571	A Based on	WO 2001096311
US 2004024216	A1 Div ex	US 6620821
JP 2004503541	W Based on	WO 2001096311
HU 2003002955	A2 Based on	WO 2001096311
MX 2002012415	A1 Based on	WO 2001096311

PRIORITY APPLN. INFO: US 2000-211594P 20000615; US 2001-875218 20010606; US 2001-8154 20011204; US 2003-602753 20030624

INT. PATENT CLASSIF.:

MAIN: A61K031-435; A61K031-4747; C07D000-00; C07D221-06; C07D221-16; C07D405-02; C07D405-06

SECONDARY: A61K031-438; A61K031-473; A61P001-00; A61P001-04; A61P001-16; A61P003-04; A61P003-06; A61P003-10;

A61P007-02; A61P009-00; A61P009-08; A61P009-10; A61P009-12; A61P015-10; A61P019-08; A61P019-10; A61P025-28; A61P029-00; A61P031-18; A61P035-00; A61P043-00; C07D221-08; C07D221-10; C07D221-18; C07D221-20; C07D221-22

BASIC ABSTRACT:

WO 200196311 A UPAB: 20020226

NOVELTY - Pyridine-containing compound is new.

DETAILED DESCRIPTION - Pyridine-containing compounds of formula (I), or their salts (when R3 is H), prodrug ester, or stereoisomer is new.

Z' = -CH(OH)-CH2-C(R7)(OH)-CH2-CO2R3 or a group of formula (i);

n = 0 or 1;

x = 0-4;

y = 0-4;

R1 and R2 = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl or cycloheteroalkyl;

R3 = H or lower alkyl;

R4 = h, halo, CF3, hydroxy, alkyl, alkoxy, alkanoylamino or cyano;

R7 = H or lower alkyl;

dashed line = single or double bond which may be cis or trans.

With the proviso that at lest one of x and y is other than 0. Optionally at least one carbons of (CH2)x and/or at least one carbon of (CH2)y together with additional carbons forms 3 - 7 membered spirocyclic ring.

INDEPENDENT CLAIMS are also included for the following:

(1) a pharmaceutical combination comprising (I) and at least one hypolipidemic agent (1), lipid-lowering agent (2), lipid agent (3), lipid modulating agent (4), at least one other type of therapeutic agent (5) including antidiabetic agent (6), anti-obesity agent (7), antihypertensive agent (8), platelet aggregation inhibitor (9), anti-dementia agent (10), anti-Alzheimer's agent (11), antiosteoporosis agent (12), and/or hormone replacement therapeutic agent (13), other cardiovascular agent (14) including anti-anginal agent (15), anti-arrhythmic agent (16), anti-atherosclerosis agent (17), anti-inflammatory agent (18), anti-arthritis agent (19), anti-platelet agent (20), anti-heart failure agent (21)), anti-cancer agent (22), anti-infective agent (23), hormone replacement agent (24), **growth hormone secretagogues** (25), selective androgen receptor modulator (26), and/or immunomodulatory agent (27); and

(2) an intermediate of formula (II);

(3) a compound of formula (V).

Q = -CO2T, CH2OH, -CH2-halO, -CH2-P(=O)(W)-W or a group of formula (ii);

asterisk = attachment point;

R3'' = H, alkali/alkaline earth metal ion, amino acid or internal lactone in the form of its sodium, calcium or arginine salt;

T = alkyl; and

W = aryl, alkyl or alkoxy.

ACTIVITY - Antilipemic; Antiarteriosclerotic; Nootropic; Neuroprotective; Osteopathic; Antiinflammatory; Cerebroprotective; Cardiant; Antianginal; Hypotensive; Anti-diabetic; Anti-tumor; Cytostatic; Antiulcer; Ophthalmological; Anti-HIV; Vasotropic; Anorectic; Gastrointestinal; Antiarrhythmic.

MECHANISM OF ACTION - Metalloprotease (MTP) inhibitor; 3-hydroxy-3-methylglutaryl-coenzyme A (HMG CoA) reductase inhibitor; squalene synthetase inhibitor; fibric acid derivative; peroxisome proliferator activated receptors (PPAR) alpha agonist; PPAR dual alpha / gamma agonist; PPAR delta agonist; acyl coenzyme A;cholesterol acyl transferase (ACAT) inhibitor; lipoxygenase inhibitor; cholesterol absorption inhibitor; ileal Na+/bile acid cotransporter inhibitor;

upregulator of low density lipoprotein (LDL) receptor activity; cholesteryl ester transfer protein inhibitor; PTP-1B inhibitor; CCKA (undefined) agonist; neuropeptide Y antagonist,

USE - (I) is used for inhibiting cholesterol biosynthesis, lowering blood serum cholesterol levels and/or modulating blood serum cholesterol levels, lowering low density lipoprotein (LDL) cholesterol and/or increasing ADL (undefined) cholesterol, treating dyslipidemia, mixed dyslipidemia, LDL Pattern B, LDL Pattern A, hyperlipidemia, hypercholesterolemia, hypo alpha -lipoproteinemia, hyperlipoproteinemia, hypertriglyceridemia and other aberrations of apolipoprotein B metabolism, reducing levels of Lp(a), other cholesterol-related diseases, progression of atherosclerosis, Alzheimer's disease, osteoporosis, osteopenia, inflammatory markers, C-reactive protein, preventing or treating low grade vascular inflammation, stroke, dementia, coronary heart disease, stable and unstable angina, peripheral vascular disease, peripheral arterial disease, acute vascular syndromes, the risk of undergoing myocardial revascularization procedures, microvascular diseases such as nephropathy, neuropathy, retinopathy and nephrotic syndrome, hypertension, Type I diabetes, Type 2 diabetes, and related diseases, insulin resistance, hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol, obesity, LDL Pattern B, LDL Pattern A, Syndrome X, diabetic complications, dysmetabolic syndrome, and related diseases, and sexual dysfunction, malignant lesions, premalignant lesions, gastrointestinal malignancies, liposarcomas and epithelial tumors, cancer induced asthenia (fatigue), irritable bowel syndrome, Crohn's disease, gastric ulceritis, and gallstones, and HIV infection, drug-induced lipodystrophy, and proliferative diseases, improving coagulation homeostasis, reducing PAI-1 activity, reducing fibrinogen, and/or reducing platelet aggregation, and/or improving endothelial function, and primary and secondary prevention of myocardial infarction, primary prevention of coronary events, or secondary prevention of cardiovascular events. Also for treating cholesterol related diseases, diabetes and related diseases, cardiovascular diseases and cerebrovascular diseases.

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B01-C06; B04-C03; B04-J03A; B04-N02; B04-N04; B05-B01E; B06-A02; B06-D02; B06-D04; B06-D06; B06-D07; B06-D09; B06-D13; B06-D16; B06-D18; B06-F03; B07-A02; B07-A02B; B07-A03; B07-D02; **B07-D03**; B07-D04C; B07-D05; B07-D06; B07-D12; B07-D13; B07-E01; B07-E04; B07-F01; B08-C01; B10-A08; B10-A13D; B10-A15; B10-A17; B10-B03B; B10-B04B; B10-C03; B10-C04B; B14-C03; B14-C09; B14-D02; B14-D03; B14-D06; B14-D07C; B14-E10; B14-F01; B14-F02; B14-F02B; B14-F06; B14-F07; B14-H01; B14-J01A4; B14-J04; B14-L06; B14-N01; B14-N03; B14-N11; B14-S04

TECH UPTX: 20020226

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: The saturated derivative of (IB) (where a is CH2-CH2) is obtained by catalytic (Pd/C, Pt/C, Pd(OH)2) hydrogenation of (IA).

Preferred Compounds: The compound is of formula (III) or its alkali metal salt, alkaline earth metal salt, amino acid salt or an acid addition salt via the pyridine of the corresponding delta lactone; formula (IV), (V) or (VI) or their salt or internal lactone in the form of calcium salt, sodium salt or arginine salt; or formula (VII) or its internal lactone in the form of its sodium salt, calcium salt or arginine salt.

R2' = alkyl or cycloalkyl;

R3' = H, alkali metal, alkaline earth metal or amino acid salt;

R5 and R6 = H, halo or alkyl.
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: (1) - (4) or (17) comprises at least one metalloprotease (MTP) inhibitor, 3-hydroxy-3-methylglutaryl-coenzyme A (HMG CoA) reductase inhibitor, squalene synthetase inhibitor, fibric acid derivative, peroxisome proliferator activated receptors (PPAR)alpha agonist, PPAR dual alpha/gamma agonist, PPAR delta agonist, acyl coenzyme A;cholesterol acyl transferase (ACAT) inhibitor, lipoxygenase inhibitor, cholesterol absorption inhibitor, ileal Na+/bile acid cotransporter inhibitor, upregulator of low density lipoprotein (LDL) receptor activity, cholesteryl ester transfer protein inhibitor, bile acid sequestrant, or nicotinic acid and their derivatives, adenine triphosphatase (ATP) citrate lyase inhibitor, phytoestrogen compound, an high density lipoprotein (HDL) upregulator, LDL catabolism promoter, antioxidant, phosphopolylipase (PLA)-2 inhibitor, antihomocysteine agent, HMG-CoA synthase inhibitor, lanosterol demethylase inhibitor, or sterol regulating element binding protein-I agent. (6) is at least one antidiabetic agent or antihyperglycemic agent including insulin **secretagogues** or insulin sensitizer, which may include biguanide, sulfonyl urea, PTP-1B inhibitor, aldose reductase inhibitor, glucosidase inhibitor, PPARgamma agonist, PPARalpha agonist, PPARdelta antagonist or agonist, aP2 inhibitor, PPAR alpha/gamma dual agonist, dipeptidyl peptidase IV (DP4) inhibitor, SGLT2 inhibitor, glycogen phosphorylase inhibitor, and/or meglitinides, insulin, and/or glucagon-like peptide-1 (GLP-1) or their mimetics (preferably metformin, glyburide, glimepiride, glipyride, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, troglitazone, rosiglitazone, insulin, Gl-262570, isaglitazone, JTT-501, NN-2344, L895645, YM-440, R-119702, AJ9677, repaglinide, nateglinide, KAD1129, AR-HO39242, GW-409544, KRP297, AC2993, LY315902, P32/98 and/or NVP-DPP-728A). (5) is a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin (and dopamine) reuptake inhibitor, an aP2 inhibitor, a thyroid receptor beta drug, an anorectic agent, a PTP-1B inhibitor, a CCKA (undefined) agonist, a neuropeptide Y antagonist, a melanocortin-4-receptor agonist, a PPAR modulator which is a PPARgamma antagonist, PPARalpha agonist, and/or PPARdelta antagonist, a leptin inhibitor such as a leptin receptor activator, a fatty acid oxidation upregulator or inducer. (4) is an MTP inhibitor, an HMG CoA reductase inhibitor, a squalene synthetase inhibitor, a fibric acid derivative, an upregulator of LDL receptor activity, a lipoxygenase inhibitor, or an ACAT inhibitor (preferably pravastatin, lovastatin, simvastatin, atorvastatin, cerivastatin, fluvastatin, pitavastatin, rosuvastatin, fenofibrate, gemfibrozil, clofibrate, avasimibe, TS-962, MD-700, cholestagel, niacin, and/or LY295427). (3) is a cholesteryl ester transfer protein inhibitor. (8) is an ACE inhibitor (preferably captopril, fosinopril, enalapril, lisinopril, quinapril, benazepril, fentiapril, ramipril or moexipril, especially ramipril), angiotensin II receptor antagonist (preferably irbesartan, losartan or valsartan), NEP inhibitor, a NEP/ACE inhibitor (preferably omapatrilat, gemopatrilat, or CGS 30440, especially omapatrilat or gemopatrilat), a calcium channel blocker, a T-channel calcium antagonist, a a-adrenergic blocker, a diuretic, a a-adrenergic blocker, a dual action receptor antagonist, or a heart failure drug (preferably amlodipine besylate, prazosin HCI, verapamil, nifedipine, nadolol, propranolol, or clonidine HCI, carvediol, atenolol, hydrochlorothiazide, torasemide, furosemide, spironolactone or indapamide). (7) is orlistat, ATL962, AJ9677, L750355, CP331648, sibutramine, topiramate, axokine, dexamphetamine, phentermine, phenylpropanolamine, and/or mazindol, P57 or CP-644673. (9) is aspirin, clopidogrel, ticlopidine, dipyridamole, ifetroban, abciximab, tirofiban, eptifibatide, or anagrelide (preferably aspirin and/or clopidogrel). (5) is (10) or (11) (preferably Cognex (RTM; tacrine HCl), Aricept (RTM;

donepezil), gamma secretase inhibtor, a beta-secretase inhibitor and/or antihypertensive agent), (12) (preferably parathyroid hormone, a bisphosphonate, alendronate, a Ca receptor agonist or a progestin receptor agonist), (13) (preferably a selective estrogen receptor modulator), a tyrosine kinase inhibitor, a selective androgen receptor modulator, (16) (preferably a beta-blocker, or a calcium channel blocker, or an a-adrenergic blocker), coenzyme Q sub. 10, an agent that upregulates type III endothelial cell nitric acid syntase, a chondroprotective compound (preferably polysulfated glycosaminoglycan, glucosamine, chondroitin sulfate, hyaluronic acid, pentosan polysulfate, doxycycline or minocycline), a cyclooxygenase (COX)-2 inhibitor (preferably Celebrex or Vioxx or a glycoprotein IIa/IIIb receptor antagonist), a 5-HT reuptake inhibitor, (25), (17), (23), an immunosuppressant for use in transplantation, or an antineoplastic agent.

ABEX UPTX: 20020226

SPECIFIC COMPOUNDS - 38 Compounds (I) are disclosed e.g. Sodium 7-(2-cyclopropyl-4-(4-fluorophenyl)-6,7-dihydro-5H-benzo(6,7)cyclohepta(1,2-b)pyridine-3-yl-3,5-dihydroxy-hept-6-enoic acid of formula (Ia).

ADMINISTRATION - (I) is administered orally or by injection in a dosage of 0.1-500 (preferably 0.2-100) mg in a single dose or 1-4 times per day.

EXAMPLE - A round bottom flask was charged with (2-Cyclopropyl-4-(4-fluoro-phenyl)-6,7-dihydro-5H-benzo(6,7)cyclohepta(1,2-b)pyridin-3-ylmethyl)-phosphonic acid diethyl ester (2.062 g) and charged with unhydrous toluene, dried and purged with argon. The residue was dissolved in THF (15 ml) and cooled to -78degreesC. A solution of n-butyl lithium (1.90 ml) was added dropwise and maintained the temperature at -78 - -74degreesC. A solution of (6-formyl-2,2-dimethyl-(1,3)-dioxan-4-yl)-acetic acid-tert-butyl ester (1.33 g) in tetrahydrofuran (THF) (10 ml) was added. The reaction mixture was stirred at -78degreesC for 40 minutes, at -10degreesC for 1 hour and at room temperature for 1 hour. The reaction mixture was quenched and extracted followed by a basic work up to give (6-(2-(2-Cyclopropyl-4-(4-fluoro-phenyl)-6,7-dihydro-5H-benzo(6,7)cyclohepta(1,2-b)pyridin-3-yl)-vinyl)-2 ,2-dimethyl-(1,3)dioxan-4-yl)-acetic acid tert-butyl ester (a). To a solution of (a) (804 mg) in dichloromethane (18 ml) at 0degreesC was added trifluoroacetic acid (1.59 ml). The reaction mixture was stirred at room temperature for 5 hours, diluted, washed, dried, filtered and concentrated followed by purification to give 6-(2-(2-Cyclopropyl-4-(4-fluoro-phenyl)-6,7-dihydro-5H-benzo(6,7)cyclohepta(1,2-b)pyridin-3-yl)-vinyl)-4-hydroxy-tetrahydro-pyran-2-one (b) (540 mg). To a solution of (b) (515 mg) in THF (10 ml) was added 1N aqueous sodium hydroxide (1.37 ml) and stirred at room temperature for 10 minutes. The reaction mixture was concentrated and purified by SP207 resin (Na+ form), and eluted. The desired fractions were lyophilized to give 7-(2-cyclopropyl-4-(4-fluorophenyl)-6,7-dihydro-5H-benzo(6,7)cyclohepta(1,2-b)pyridine-3-yl-3,5-dihydroxy-hept-6-enoic acid (91%).

DEFINITIONS - Preferred Definitions:
dashed line = double bond which is trans;
R1 = aryl (preferably 4-fluorophenyl, 4-fluoro-3-methylphenyl or 3,5-dimethylphenyl);
R2 = alkyl, cycloalkyl or aryl;
R4 = H;
n = 0;
x = 3; and
y = 0.

L115 ANSWER 27 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-116720 [10] WPIX
DOC. NO. CPI: C2000-035691
TITLE: Pharmaceutical composition for treating musculoskeletal frailty including osteoporosis, osteoporotic fracture, low bone mass, frailty and low muscle mass.
DERWENT CLASS: B02 B03
INVENTOR(S): KE, H Z; LI, M; PAN, L C; THOMPSON, D D
PATENT ASSIGNEE(S): (PFIZ) PFIZER PROD INC
COUNTRY COUNT: 84
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 9965488	A1	19991223	(200010)*	EN	31	A61K031-44
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW						
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW						
AU 9933420	A	20000105	(200024)			A61K031-44
ZA 9903973	A	20010228	(200114)		27	A61K000-00
BR 9911357	A	20010313	(200118)			A61K031-44
EP 1085867	A1	20010328	(200118)	EN		A61K031-44
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MK NL PT RO SE SI						
NO 2000006381	A	20001214	(200118)			A61K031-444
CZ 2000004680	A3	20010613	(200138)			A61K031-40
CN 1305378	A	20010725	(200164)			A61K031-44
MX 2000012628	A1	20010401	(200171)			A61K031-44
KR 2001052817	A	20010625	(200173)			A61K031-44
SK 2000001890	A3	20011203	(200203)			A61K031-44
HU 2001002395	A2	20011128	(200209)			A61K031-437
JP 2002518328	W	20020625	(200243)		41	A61K031-444

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9965488	A1	WO 1999-IB796	19990503
AU 9933420	A	AU 1999-33420	19990503
ZA 9903973	A	ZA 1999-3973	19990615
BR 9911357	A	BR 1999-11357	19990503
		WO 1999-IB796	19990503
EP 1085867	A1	EP 1999-914723	19990503
		WO 1999-IB796	19990503
NO 2000006381	A	WO 1999-IB796	19990503
		NO 2000-6381	20001214
CZ 2000004680	A3	WO 1999-IB796	19990503
		CZ 2000-4680	19990503
CN 1305378	A	CN 1999-807381	19990503
MX 2000012628	A1	MX 2000-12628	20001215
KR 2001052817	A	KR 2000-714140	20001213
SK 2000001890	A3	WO 1999-IB796	19990503
		SK 2000-1890	19990503
HU 2001002395	A2	WO 1999-IB796	19990503
		HU 2001-2395	19990503
JP 2002518328	W	WO 1999-IB796	19990503
		JP 2000-554368	19990503

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9933420	A	Based on	WO 9965488
BR 9911357	A	Based on	WO 9965488
EP 1085867	A1	Based on	WO 9965488
CZ 2000004680	A3	Based on	WO 9965488
SK 2000001890	A3	Based on	WO 9965488
HU 2001002395	A2	Based on	WO 9965488
JP 2002518328	W	Based on	WO 9965488

PRIORITY APPLN. INFO: US 1998-89424P 19980616
INT. PATENT CLASSIF.:
MAIN: A61K000-00; A61K031-40; A61K031-437; A61K031-44; A61K031-444
SECONDARY: A61P001-02; A61P019-00; A61P019-08; A61P019-10; A61P043-00
ADDITIONAL: C07D295-08; C07D471-04

BASIC ABSTRACT:

WO 9965488 A UPAB: 20000228

NOVELTY - A pharmaceutical composition comprises a first compound, (-)-cis-6-phenyl-5-(4-(2- pyrrolidin-1-yl-ethoxy)-phenyl)-5,6,7,8-tetra hydronaphthalene-2-ol or its salt and a second compound, 2-amino-N-(1(R)-(2,4-difluorobenzyl oxymethyl)-2-oxo-2-(3-oxo-3a(R)-pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo(4,3-c)pyridin-5-yl)-ethyl)-2-methyl-propionamide (sic) or its salt.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(A) a method for treating a mammal suffering from musculoskeletal frailty comprising administering the pharmaceutical composition; and

(B) a kit comprising (a) (-)-cis-6-phenyl-5-(4-(2-pyrrolidin-1-yl-ethoxy)-phenyl)-5,6,7,8-tet rahydronaphthalene-2-ol or its salt and a carrier or diluent in a first unit dosage form and (b) 2-amino-N-(1(R)-(2,4-difluorobenzyl oxymethyl)-2-oxo-2-(3-oxo-3a(R)-pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo(4,3-c)-pyridin-5-yl)-ethyl)2-methyl-propionamide (sic) or its salt and a carrier or diluent in a second unit dosage form; and (c) a container.

ACTIVITY - Osteopathic.

MECHANISM OF ACTION - Selective estrogen receptor modulator and **growth hormone secretagogue.**

Tests are described but no results were given for claimed compounds.

USE - The composition is used for treating a mammal, preferably human, suffering from osteoporosis, osteotomy, childhood idiopathic bone, bone loss associated with periodontitis or musculoskeletal frailty (claimed).

ADVANTAGE - Bone healing following facial reconstruction, maxillary reconstruction or mandibular reconstruction is treated, vertebral synostosis is induced or long bone extension is enhanced, the healing rate of a bone graft is enhanced or prosthetic ingrowth is enhanced (claimed). The use of the pharmaceutical compositions results in a more rapid and higher magnitude bone mass gain. The combinations increase bone density and muscle mass while reducing fat mass and total serum cholesterol. They increase bone mass and decrease fracture rates.

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FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: B06-D08; **B07-D03**; B14-C09A

ABEX UPTX: 20000228

SPECIFIC COMPOUNDS - The first compound is (-)-cis-6-phenyl-5-(4-(2-pyrrolidin-1-yl-ethoxy)-phenyl)-5,6,7,8-tetra hydronaphthalene-2-ol D-tartrate and the second compound is 2-amino-N-(1(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-(3-oxo-3a(R)-pyridin-2-ylmethyl)-2-(2,2,2-trifluoro-ethyl)- 2,3,3a,4,6,7-hexahydro-pyrazolo(4,3-c)pyridin-5-yl)-ethyl)-2-methyl-propionamide L-tartrate (sic).

ADMINISTRATION - First and second compounds are administered simultaneously, preferably the second compound is administered for 3 months - 3 years followed by administration of the first compound from 3 months - 3 years without the second compound after the 3-year administration of second compound (claimed). Administration may be systemic and/or local. It may be oral, parenteral or intraduodenal. Parenteral may be intravenous, intramuscular, trans- or subcutaneous or intramedullary. Dosage for the first compound is 0.0001 - 100 (preferably 0.001 - 10) mg/kg/day. Dosage for the second compound is 0.0001 - 100 (preferably 0.01 - 5) mg/kg/day.

L115 ANSWER 28 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 1997-042703 [04] WPIX
DOC. NO. CPI: C1997-013482
TITLE: New di peptide cpds. - used to increase levels of endogenous **growth hormone** and to treat osteoporosis.
DERWENT CLASS: B02 B03
INVENTOR(S): CARPINO, P A; DASILVA JARDINE, P A; LEFKER, B A; RAGAN, J A; JARDINE, P A; LECKER, B A; JARDINE, P A D; DASILVA-JARDINE, P A
PATENT ASSIGNEE(S): (PFIZ) PFIZER INC
COUNTRY COUNT: 25
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 9638471	A1	19961205	(199704)*	EN	174	C07K005-02
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE						
W: CA FI JP MX US						
NO 9602162	A	19961202	(199706)			C07K005-02
AU 9654554	A	19961212	(199707)			C07K005-06
FI 9704368	A	19971128	(199808)			C07K000-00
EP 828754	A1	19980318	(199815)	EN		C07K005-02
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE						
JP 10510511	W	19981013	(199851)		247	C07D207-16
US 5936089	A	19990810	(199938)			A61K031-475
MX 9709278	A1	19980301	(200002)			C07K005-02
CN 1143647	A	19970226	(200062)			C07K005-06
JP 3133073	B2	20010205	(200110)		93	C07D207-16
CA 2220055	C	20010424	(200128)	EN		C07K005-078
MX 201996	B	20010522	(200227)			C07D205-00

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9638471	A1	WO 1995-IB410	19950529
NO 9602162	A	NO 1996-2162	19960528
AU 9654554	A	AU 1996-54554	19960528
FI 9704368	A	WO 1995-IB410	19950529
		FI 1997-4368	19971128

EP 828754	A1	EP 1995-918123	19950529
		WO 1995-IB410	19950529
JP 10510511	W	WO 1995-IB410	19950529
		JP 1996-511175	19950529
US 5936089	A	WO 1995-IB410	19950529
		US 1997-973268	19971126
MX 9709278	A1	MX 1997-9278	19971128
CN 1143647	A	CN 1996-107637	19960528
JP 3133073	B2	WO 1995-IB410	19950529
		JP 1996-511175	19950529
CA 2220055	C	CA 1995-2220055	19950529
		WO 1995-IB410	19950529
MX 201996	B	MX 1997-9278	19971128

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 828754	A1	Based on	WO 9638471
JP 10510511	W	Based on	WO 9638471
US 5936089	A	Based on	WO 9638471
JP 3133073	B2	Previous Publ.	JP 10510511
		Based on	WO 9638471
CA 2220055	C	Based on	WO 9638471

PRIORITY APPLN. INFO: WO 1995-IB410 19950529
REFERENCE PATENTS: WO 9411012; WO 9413696; WO 9509633; WO 9511029
INT. PATENT CLASSIF.:
MAIN: A61K031-475; C07D205-00; C07D207-16; C07K000-00; C07K005-02; C07K005-06; C07K005-078
SECONDARY: A61K031-395; A61K031-40; A61K031-445; A61K031-47; A61K031-495; A61K031-505; A61K031-535; A61K038-00; A61K038-05; A61K038-08; A61K038-18; A61K038-25; A61K038-30; A61P005-06; A61P043-00; C07D207-00; C07D207-14; C07D209-00; C07D209-44; C07D211-04; C07D211-16; C07D211-52; C07D211-58; C07D215-00; C07D217-00; C07D217-02; C07D217-06; C07D217-22; C07D217-24; C07D223-00; C07D225-00; C07D401-00; C07D401-04; C07D401-06; C07D401-12; C07D401-14; C07D405-14; C07D409-06; C07D409-14; C07D413-06; C07D413-14; C07D417-14; C07D471-04; C07D487-04; C07D498-04; C07K005-023; C07K005-027; C07K005-03; C07K005-033; C07K005-065; C07K005-08; C07K005-083

BASIC ABSTRACT:

WO 9638471 A UPAB: 19970122
Heterocyclic di-peptide cpds. of formula (I) and their salts and diastereomers are new in which: Z=COCR1R2cLCOANR4R5; L = opt. substd. N, O or CH2; W = H; or W+X = complete an opt. substd. fused benzene ring; Y = e.g. H, 1-6 C alkyl or 4-10 C cycloalkyl; X = e.g. OR2, R2, N(R50M)(Aryl), R9R8N-C(O) or R2bOC(O); R1 = e.g. 1-10 C alkyl, aryl, aryl(1-6 C alkyl) or 3-7 C cycloalkyl-(1-6 C alkyl); R2c = H, 1-6 C alkyl or 3-7 C cycloalkyl; or R2c+R1 = 3-8 C ring opt. including O, S or NR2a; R2 = H, 1-6 C alkyl, 3-7 C cycloalkyl or 1-6 C haloalkyl; R2a = H or 1-6 C alkyl; R2b = H, 1-8 C alkyl, 1-8 C haloalkyl, 3-8 C cycloalkyl, alkaryl or aryl; R4, R5 = H, 1-6 C alkyl opt. substd. by 1-5 halo, 1-3 OH, 1-3 1-10 C alkanoyloxy, 1-3 1-6 C alkoxy, Ph, PhO, 2-furyl, 1-6 C alkoxycarbonyl or S(O)m(1-6 C alkyl); or R4+R5 = (CH2)rLa(CH2)s; La = C(R2)2, S(O)m or NR2; r, s = 1-3; R50 = 4-morpholino, 4-(1-methylpiperazinyl), 3-7 C cycloalkyl or 1-6 C alky l, all opt. substd. by 1-3 of F, OH, OMe, OCF3, CF3 and 3-7 C cycloalkyl; M = C(O) or SO2; A = bond or Z1(CH2)x-C(R7)(R7a)-(CH2)y; x, y

= 0-3; Z1 = NR2, O or bond; R7, R7a = H, CF3, Ph, 1-6 C alkyl opt. substd. by imidazolyl, Ph, indolyl, p-hydroxyphenyl, OR2, S(O)mR2, CO2R2, 3-7 C cycloalkyl, N(R2)2, or CON(R2)2; or R7 and R7a can be independently joined to R4 and/or R5 to form 1-5 C alkylene bridges between the terminal N and the alkyl of R7 and R7a; or R7+R7a = 3-7 membered ring; R9 = H or 1-6 C alkyl, Ph, thiazolyl, imidazolyl, furyl or thienyl, all opt. substd. by 1-3 of Cl, F, Me, OMe, OCF3 and CF3; R8 = H, 1-6 C alkyl opt. substd. by 1-5 halo, 1-3 OH, 1-3 1-10 C alkanoyloxy, 1-3 1-6 C alkoxy, Ph, PhO, 1-6 C alkoxycarbonyl or S(O)m-(1-6 C alkyl); or R8+R9 = (CH2)rLa'(CH2)s; La' = C(R2)2, S(O)m O or NR2; and m, n = 0-2. N.B. In the disclosure, the definition of La further includes O.

USE - (I) are used to increase levels of endogenous **growth hormone** and in treatment of osteoporosis. Pharmaceutical compsns. contain (I) opt. in combination with a **growth hormone secretagogue** selected from GHRP-6, Hexarelin, GHRP-1, **growth hormone** releasing factor (GRF), IGF-1, IGF-2 or B-HT920, or, for treatment of osteoporosis, with a bisphosphonate cpd. e.g. alendronate (all claimed). (I) can be administered to animals to increase their rate and extent of growth and their milk production. (I) are used for stimulating release of endogenous **growth hormone** (GH) in elderly patients, treating GH-deficient adults, preventing catabolic side-effects of glucocorticoids, stimulating immune system, accelerating wound-healing, accelerating bone fracture repair, treating growth retardation, treating acute or chronic renal failure or insufficiency, treating physiological short stature including GH-deficient children, treatment of obesity, accelerating recovery of burns patients; treating intra-uterine growth retardation, skeletal dysplasia, hypercortisonism or Cushings syndrome; replacement of GH in stressed patients; treating osteochondrodysplasias, Noonans syndrome, sleep disorders, Alzheimer's disease and psychosocial deprivation; and reducing cachexia and protein loss due to e.g. cancer or AIDS.

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FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B06-H; B07-D01; **B07-D03**; B07-D05; B07-D06; B14-D01E; B14-N01

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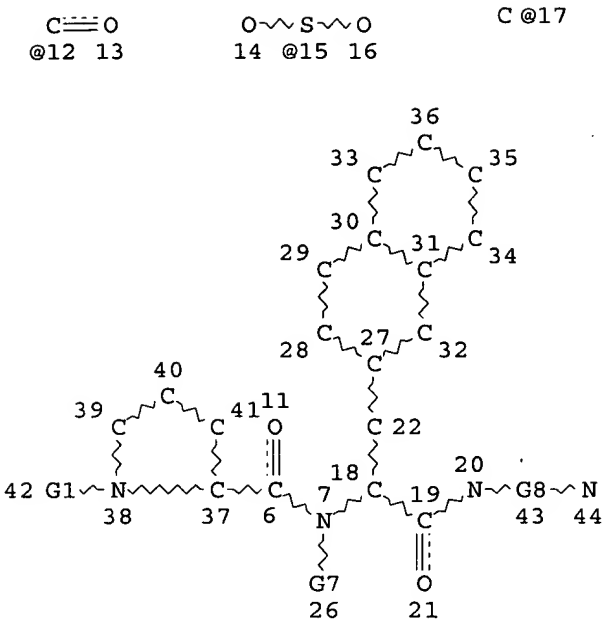

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DEFAULT MLEVEL IS ATOM
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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 33

STEREO ATTRIBUTES: NONE
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L80 1 SEA FILE=BEILSTEIN ABB=ON PLU=ON L79 NOT RN/FA

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L80 ANSWER 1 OF 1 BEILSTEIN COPYRIGHT 2005 BEILSTEIN MDL on STN

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Molec. Formula (MF): C78 H104 N20 O15
Molecular Weight (MW): 1561.80
Lawson Number (LN): 27812, 26264, 16193, 16098, 16048, 3487, 3408, 3407, 3400, 3379, 1762
File Segment (FS): Stereo compound
Compound Type (CTYPE): heterocyclic
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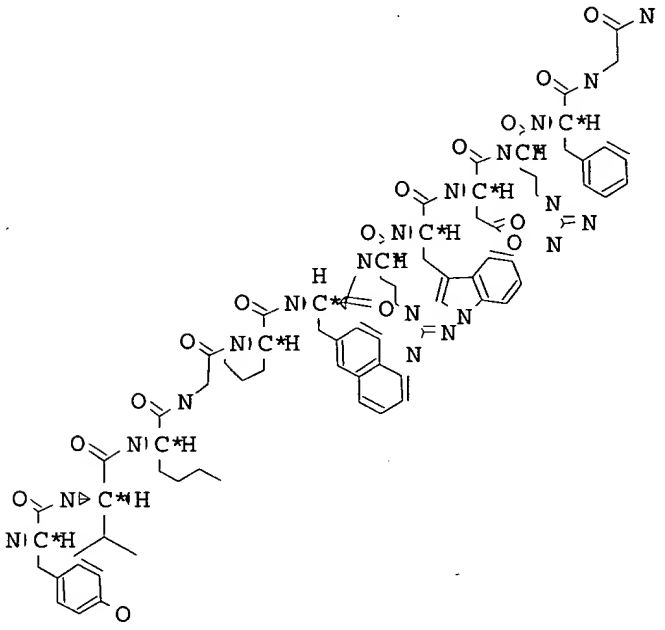
Entry Date (DED): 2004/04/23
Update Date (DUPD): 2004/04/23



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ED	Entry Date	1
UPD	Update Date	1
PHARM	Pharmacological Data	6

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